Exposure to Nonhuman Primates: Situation, Reference and Intervention Guide

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Professional Practice Guide

Exposure to Nonhuman Primates: Situation, Reference and Intervention Guide

Direction des risques biologiques
et de la santé au travail

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FOREWORD

In 2002, the Table de coordination nationale de maladies infectieuses tasked a multisectoral working group with the development of a professional practice and intervention guide for persons who work with nonhuman primates. In 2010, the Table asked the Institut national de santé publique du Québec (INSPQ) to publish the guide and make it available to the public.

This guide is intended primarily for public health professionals, clinicians, emergency physicians, veterinary physicians, and occupational health and safety physicians who work in the organizations concerned with the exposure to nonhuman primates (including physicians responsible for occupational health in the public system).

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES AND ALGORITHMS

LIST OF INITIALISMS AND ACRONYMS

CDC	Centers for Disease Control and Prevention
CFIA	Canadian Food Inspection Agency
DSP	Direction de santé publique
INSPQ	Institut national de santé publique du Québec
LSPQ	Laboratoire de santé publique du Québec
MAPAQ	Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec
MSSS	Ministère de la Santé et des Services sociaux
NML	National Microbiology Laboratory
PHAC	Public Health Agency of Canada

1 ISSUE

Exposures to nonhuman primates usually involve bites. Nonhuman primate bites are thought to be more serious and more likely to become infected than other exotic animal bites (Goldstein, 1992). Even with the administration of antibiotic prophylaxis, simian bites frequently lead to bacterial infections and complications (Goldstein et al., 1995).

However, the most important reason for developing an intervention guide for the management of bites and percutaneous and mucosal exposures to the bodily fluids of nonhuman primates is the risk of contracting B Virus infection, which is endemic among macaques and can be fatal when contracted by humans. Other viral transmission risks include rabies and tetanus.

No vaccines or specific immunoglobulins are presently available to prevent B Virus infection in humans, although antiviral agents can be administered. Infection prevention in humans therefore rests on the application of strict hygiene and prevention measures, immediate disinfection of the exposure site, and administration of prophylaxis as required.

In Québec, exposures to nonhuman primates occur primarily in research laboratories that use animal models, particularly species that are part of the genus Macaca. Exposures also occur with pets, although the sale of monkeys as companion animals is against the law (Fournier and Levesque, 2001). The high prevalence of B Virus in macaques, not to mention the species' tendency to bite, make them unsuitable as pets (Ostrowski et al., 1998). Exposure can also occur in the context of travel abroad.

Several reports of simian bites in and around Montréal, Lanaudière and Montérégie have given rise to questions concerning the measures that should be taken in such situations and the role of responders. This Guide is designed to serve as a reference tool for medical personnel who provide care to persons who are exposed to nonhuman primate. Although its focus is the prevention of B Virus infection, this Guide also provides information on the prevention of other infectious diseases that can be transmitted by nonhuman primates.

Many people work with nonhuman primates in Québec, in the context of research laboratories, parks or zoos. Relevant prevention measures are not always known or applied in these settings (Brunet, 1998). The Guide will provide support for those who must intervene when exposures occur in workplaces that have no procedures to deal with such situations. It will also provide a means of adjusting existing prevention measures to ensure that they are in line with current recommendations.

In developing the guide, the working group undertook a review of the literature on the subject, including existing guides. The various stakeholders concerned were also consulted by the working group in order to establish their respective responsibilities (MSSS, DSP, INSPQ, MAPAQ).

This intervention guide reviews the conditions and epidemiology of B Virus transmission, the prevention and treatment of infection in humans, the prevention of other communicable nonhuman primate diseases, and the application of general preventive measures.

2 B VIRUS INFECTION IN HUMANS

2.1 BIOLOGY OF B VIRUS

2.1.1 Nomenclature used

Macacine herpesvirus 1 is the term used in the nomenclature of the International Committee on Taxonomy of Viruses. The English-language literature contains a number of synonyms, including “B Virus,” “Herpesvirus simiae,” “Simian herpes B virus,” “herpes virus B,” “Cercopithecine herpesvirus 1” and “monkey B Virus.” B Virus is part of the family *Herpesviridae*, sub-family *Alphaherpesvirinae*, and genus *Simplexvirus*. This designation is based on the virological characteristics of the virus and its serological cross-reactivity with other simplex virus virions that are endemic in humans, such as HSV-1 and HSV-2 (Huff and Barry, 2003). In this document the term “B Virus” will be used.

2.1.2 Physicochemical and biological properties

Due to its lipid envelope, B Virus is sensitive to detergents and lipid solvents; it is less stable in an acid pH environment than in a neutral pH environment. Its persistence on inanimate objects is variable and dependent on ambient temperature (Weigler, 1992; Hilliard, 1996; Health Canada, 2001). Some reports suggest that B Virus can survive for up to 7 days at room temperature (up to 37°C) or for weeks at 4°C and that it remains very stable at -70°C. However, the Committee on Occupational Health and Safety in the Care and Use of Nonhuman Primates indicates that the viability of the virus is at most 24 hours in a dry state or when exposed to sunlight (ILAR, 2003).

The viral multiplication cycle is rapid both in vivo and in cell culture. Infection leads to the destruction of infected cells and becomes latent in the nerve ganglia. Dissemination of the virus to and from the nerve ganglia is effected through axonal transport. Latency is characterized by cessation of replication and limited viral transcription. Periodic reactivation delivers the virus to mucosal epithelial cells, where it replicates anew and is released in the form of infectious virions (Huff and Barry, 2003).

2.2 EPIDEMIOLOGY OF B VIRUS

2.2.1 Exposure to nonhuman primates

In the absence of a provincial mandatory reporting system for animal bites, it is difficult to obtain accurate data on the incidence and related complications of nonhuman primate bites. Although most exposures occur within Canada, a certain number of cases do occur in the context of foreign travel.

Several viruses can be transmitted through bites or other forms of exposure to nonhuman primates. Of these, B Virus is of greatest concern since it is considered to be extremely pathogenic in humans (Whitley, 1996). The forms of exposure that can lead to viral transmission are listed in Table 1 on page 7 (Cohen et al., 2002).

B Virus is found naturally and is endemic in primate species of the genus Macaca, such as *Macaca mulatta*, *M. fascicularis*, *M. radiata*, *M. arctoides* and *M. nemistrina*. Macaques are part of a genus of primates that has an extremely large habitat. They can be found in Morocco, Algeria, Gibraltar, Afghanistan, India, China, Japan, Southeast Asia in its entirety, from the Philippines to Borneo, and Indonesia (Sumatra, Java and Sulawesi) (Bennett et al., 1995). To summarize, macaques are nonhuman primates indigenous to areas outside the Americas (Africa, Asia, Europe and Australia).

With the exception of the island of Puerto Rico in the Caribbean, where rhesus macaques were introduced by humans (Jensen et al., 2004), the nonhuman primates of the Americas (countries listed in Appendix 1) that live in their natural habitat are unlikely to carry the B Virus, since they belong to species that are not part of the genus Macaca.

However, New World species and Old World non-macaque species that have been kept in captivity with macaques for more than a week are also considered potential B Virus carriers.

Since the vast majority of nonhuman primates used in research are part of the genus Macaca, all nonhuman primates kept in captivity in laboratories or other confined spaces (including primates from colonies known to be free of the virus) are classified as macaques and potential carriers and transmitters of the virus (Huff and Barry, 2003; ILAR, 2003).

It is important to note that the risk of virus shedding is increased in macaques under the following conditions:

- animals that have undergone severe stress in recent weeks (surgery, gestation, parturition, new environment);
- animals in the mating period;
- animals that have experienced changes in their physical or social environment;
- animals that are immunocompromised;
- symptomatic animals (having lesions or signs consistent with B Virus infection);
- animals that are ill or convalescing.

2.2.2 Reported cases of B Virus infection in humans

It is estimated that several hundred occupational exposures (bites or other forms of exposure) occur each year in the United States (ILAR, 2003); fortunately, infection is extremely rare in humans.

Since its isolation in 1933, B Virus has caused approximately thirty human fatalities world-wide (CDC and NIH, 2007). Fifty cases of human infection have been identified and 26 of them are well-documented (Cohen et al., 2002).

Close to a quarter of all cases of human B Virus infection were reported between 1956 and 1958, including two fatal infections in Canada (Nagler and Klotz, 1958). The high incidence of infection during that period was due to the massive use of young rhesus macaques to

produce polio vaccine. At that time, nonhuman primates were being captured unsedated[1] (Florence, 1996; Weigler, 1992).

A resurgence of cases (nine in total) occurred between 1987 and 1994, as a result of the increased use of macaques to study AIDS and infectious hepatitis.

Although travellers frequently come into contact with monkeys in their natural habitat, no cases of transmission were documented in this context until 2009. That year, a clinical case of B Virus infection was reported in a young girl who had come into contact with a macaque in Thailand (Ritz et al., 2009).

Another clinical case was reported in a person who was bitten by a grivet monkey (non-macaque) in a national park in Africa (Mafuko Nsabimana et al., 2008).

2.2.3 Reported cases of B virus infection in nonhuman primates

The virus is well-adapted to its macaque host, in which it generally causes only benign oral lesions. As with many herpes viruses, primary infection is followed by a latency period in which the virus persists for life in the cells of the sensory ganglia; when reactivated, the virus may be found in salivary, ocular and genital secretions (Jainkittivong and Langlais, 1998; Cohen et al., 2002). In most cases, the animal is asymptomatic and viral shedding only lasts a few hours. Shedding may occur for a longer period during the primary infection or in the presence of secondary disease, in which case it may last four to six weeks (Hilliard and Scinicariello, 1992). Although rare, fatal cases of disseminated infection have been reported in macaques (Anderson et al., 1994; Simon et al., 1993; Weigler, 1992). The recent literature attributes these generalized infections to immune suppression caused by type D simian retrovirus (Carlson et al., 1997). Experimental M. fascicularis infection (in cynomolgus macaques) has shown that the virus can be isolated in the oral cavity six days after inoculation, even in the absence of visible lesions (Lee et al., 1991).

The disease has also been inoculated experimentally in American primates such as capuchin and marmoset monkeys (Florence, 1996; CDC, 1987). Although highly unlikely in the wild, natural transmission of the virus to species other than macaques has been reported. This type of accidental transmission can occur in zoos or pet shops where different species are kept in close proximity. Primate species of the genera Erythrocebus, Colobus and Cercopithecus are extremely sensitive to the virus through both direct and indirect contact and close to half of the individuals who experience such contact succumb to a disseminated infection (Loomis et al., 1981; Wilson et al., 1990). Studies of such cases show a very brief incubation period (less than two weeks) once the source of infection or the contact with a macaque has been identified. A small proportion of these non-macaque primates survive the infection. Studies have shown that these survivors shed the virus during symptomatic periods (with the presence of mouth ulcers) and continue to do so for many years after the primary infection (Thompson et al., 2000).

[1] No tranquilizer was administered.

While macaques are the species most likely to become infected, cases of infection have been documented in other primate species (Mafuko Nsabimana et al., 2008).

2.3 TRANSMISSION OF B VIRUS TO HUMANS

The bodily fluids most likely to transmit the virus from primate to human are saliva and fluid from herpetic vesicles or ulcers (CDC, 1987). Monkeys can also shed the virus through the urogenital tract or through conjunctival fluid. Other fluids or substances, such as feces and urine, may also constitute a source of contamination (CDC, 1987). Blood poses a lesser risk since viremia rarely occurs in healthy animals (Cohen et al., 2002). Exposure to saliva, blood, tissue, or cell cultures (occurring primarily through bites, scratches, and incidents/injuries involving needles, instruments or equipment) is the predominant form of transmission. Approximately 85% of all cases of human transmission occur in this way (Table 1, page 7). Other reported cases include two cases in which transmission likely occurred through exposure to droplets and one case of human-to-human transmission (a woman with eczema had applied ointment to her infected husband's vesicular lesions (Florence, 1996; Cohen et al., 2002).

Table 1 Documented cases of B Virus infection in humans (Cohen et al., 2002)

Type of exposure	Number of cases
Monkey bite	10
Monkey scratch	2
Wound contaminated with monkey saliva	1
Tissue culture-bottle cuts[a] (Hummeler et al., 1959)	1
Needlestick injury[b]	2
Possible aerosol[c]	2
Cleaned monkey skull (without gloves) (Davidson and Hummeler, 1960)	1
Needle scratch and monkey bite	1
Cage scratch	2
Possible reactivation of B virus	1
Human-to-human contact[d]	1
Mucosal splash[e]	1
Unknown	1
Total	**26**

[a] Culture involved monkey kidney cells for the production of polio vaccine.

[b] In one case, a needle had been used to inject the tissues around the eye and, in the other case, a needle may have been used previously to inject monkey.

[c] In one case, aerosolization occurred during a macaque autopsy; in the other, the patient presented with respiratory symptoms.

[d] The patient applied cream to her husband's herpes vesicles and to areas of her own skin that were affected by contact dermatitis.

[e] The patient was splashed in the eye with material, possibly feces, from a macaque.

2.4 CLINICAL ASPECTS OF B VIRUS INFECTION

2.4.1 In humans

The incubation period ranges from two days to six weeks (Florence, 1996; CDC, 1998, Cohen et al., 2002), but symptoms usually manifest within three weeks of exposure (CDC, 1987; CDC, 1988; Florence, 1996; Cohen et al., 2002; Huff and Barry, 2003). Disease development and progress depend on the inoculation site and the quantity of inoculum. In most cases, infection causes rapidly ascending encephalomyelitis (Cohen et al., 2002) Encephalomyelitis follows upon a non-specific febrile phase and is associated to varying degrees with herpetic vesicles or peripheral neurological signs.

In the infected human, B Virus multiplies at the inoculation site, which may result in the appearance of vesicles at this site. Other local symptoms may also be present, including tingling, itching, pain and numbness. Some patients have no symptoms at the inoculation site, while others may develop proximal lymphadenopathy. Within three weeks of exposure, paresthesia may develop and spread from the affected extremity. Other accompanying symptoms can include fever, myalgia, weakness in the affected limb, abdominal pain, sinusitis and conjunctivitis. Other organs, such as the lungs and liver, may also be affected.

The virus spreads through the nerves of the peripheral nervous system to the spinal cord and brain. The infection then presents as meningismus, nausea, vomiting, persistent headaches, confusion, diplopia, dysphagia, vertigo, dizziness, dysarthria, cranial nerve paralysis and ataxia. Convulsions, hemiplegia, hemiparesis, ascending paralysis, respiratory distress and coma characterize the more advanced stage of infection, as the patient evolves toward diffuse encephalomyelitis. This is different from the presentation of herpes simplex infection, where encephalitis is focal. A summary of the different symptomatic phases is presented in Table 2 (page 9).

In the absence of treatment, B Virus infection is fatal in 80% of cases. The fatality rate decreases with the use of antivirals (Cohen et al., 2002).

It is important to recall that all Alphaherpesvirinae are capable of latency and reactivation in their respective hosts. In a seroprevalence study conducted in 1995 (ILAR, 2003) among 321 persons working with nonhuman primates, no evidence of latent infection was reported. Furthermore, no seroconversion was observed among the contacts of persons infected with B Virus. It is also noteworthy that no asymptomatic seroconversion has been reported in the literature to date (Cohen et al., 2002; Straus, 2005).

Given that hundreds of exposures occur annually and in light of the technological advances that have occurred during the past decade in B Virus detection and blood screening, it can safely be stated that latency in humans in the absence of prior clinical manifestations is highly improbable (Huff and Barry, 2003).

Table 2 Clinical manifestations suggesting active infection with B virus (Holmes et al., 1995)

Early manifestation (inconsistently present) [the virus multiplies at the inoculation site]
Vesicular eruption or ulcerations at (or near) the exposure site
Severe pain or itching at the exposure site
Regional lymphadenopathy
Intermediate manifestation (inconsistently present) [the virus spreads via the peripheral nervous system and the spinal cord and reaches the brain]
Fever
Numbness, paresthesia or other neuresthesias at (or near) the exposure site, with or without proximal progression
Muscle weakness or paralysis in the exposed extremity (proximal to the inoculation site)
Conjunctivitis
Persistent hiccups
Late manifestation (avoidable with early therapy) [development of diffuse encephalomyelitis]
Sinusitis
Neck stiffness
Headache lasting more than 24 hours
Nausea and vomiting
Brain-stem findings: diplopia, dysarthria,dysphagia, dizziness, cross-hemiparesis, cerebellar signs with ataxia, crossed sensory loss, cranial nerve palsies or drop attacks
Altered mentation
Other signs compatible with central nervous system impairment or viral encephalitis including urinary retention, respiratory failure, convulsions, twitching, hemiparesis, hemiplegia,other localized neurological signs, progressive ascending paralysis or coma

2.4.2 In nonhuman primates

The incubation period of the disease is variable in primates. Although many primate species are susceptible to the virus, severity of infection varies considerably between species.

In a small number of non-macaque primate species in which B Virus infection has been documented, the disease progresses rapidly (less than 2 weeks) and tends to be disseminated rather than localized, with infection of the oral and ocular mucosa, liver, kidneys and lungs. Close to half of these cases ultimately succumb to secondary septicemia (Loomis et al., 1981; Wilson et al., 1990; Thompson et al., 2000; Mafuko Nsabimana et al., 2008).

Only a small number of cases of fatal encephalitis have been reported in macaques. Infection is most often **asymptomatic**, although symptoms similar to those described in human B Virus infection may manifest, including:

- conjunctivitis;
- vesicles at the back of the tongue, in the oral cavity, at the mucocutaneous junction of the lip, and on the genital mucosa.

It is important to note that herpetic lesions appear in only 0.7% of an infected macaque population (Florence, 1996). Infection induces a carrier state, although the animal is only intermittently contagious and may not necessarily present with herpetic lesions (CDC, 1987; Cohen et al., 2002). Drawing on studies conducted in the 1950s, recent authors have estimated that, on any given day, 2% of the members of a B Virus-infected macaque group shed the virus (Cohen et al., 2002). No study using more modern viral screening methods has been published since that time. It another case involving seven non-occupational exposures, two-thirds of the implicated macaques were seropositive (Hogan et al., 2009).

The likelihood that a macaque will be seropositive for B Virus depends on the animal's origin, age and living environment. Studies have shown that when primates of different origins live in groups, the carrier rate for individuals aged five years or more ranges between 51% and 94% (Nguyen and Lalonde, 1990; Kessler and Hilliard, 1990; CDC, 1998). In these groups, individuals under three years of age had lower rates of infection, ranging from 12% (Orcutt et al., 1976) to 28% (Zwartouw et al., 1984). According to Cohen et al. (2002), the carrier rate is 100% among nonhuman primates aged two years or more and 20% in those under age two. Obviously, the prevalence of infection and transmission is much higher when primates live in groups rather than in separate cages (Weigler, 1992).

Natural B Virus transmission between macaques occurs primarily through bites and scratches, but also through sexual activity among postpubertal animals (Weigler, 1992; Weigler et al., 1993; ILAR, 2003).

Epidemiological studies tend to show that B Virus infection is primarily acquired around the age when macaques reach sexual maturity. Moreover, vertical transmission from gestating female to fetus is also possible. The virus has been isolated in a seven-day-old macaque of the species *Macaca nemestrina* (Anderson et al., 1994) and in a four-month-old *Macaca mulatta* (Weigler et al., 1993). Maternal immunity renders newborns seropositive for 3 months up to 5½ months (Florence, 1996).

Generally speaking, New World monkeys (macaque or other species) (Appendix 1) living in their natural habit have a lower risk of B Virus infection (see 2.2.3). But all Old World monkeys and all New World monkeys kept in captivity (in laboratories or other settings) should be considered unsafe and at risk of being infected. Furthermore, all macaques (including those certified to be B Virus-free) should be considered infected owing to certain characteristics of the disease (prolonged latency, viral shedding in the absence of signs and symptoms) and the technical limitations of laboratory tests (ILAR, 2003).

Infection in macaques is equivalent to *herpes simplex* 1 and 2 in humans (e.g., labial herpes, genital herpes).

3 PREVENTION AND TREATMENT OF B VIRUS INFECTION AND OTHER INFECTIONS IN HUMANS

Exposure to a nonhuman primate or with any other wild animal can cause a number of different infections. B Virus infection is a zoonose that warrants particular attention given the severe illness it causes in humans. Consequently, any potential exposure to B Virus is considered an emergency. Infection in humans leads to deadly encephalomyelitis in 80% of cases if left untreated. In the United States, it is estimated that several hundred significant exposures (bites and other exposures) occur each year, although few people ever become infected. Cohen et al. (2002) estimate that 0.4% to 2.0% of significant exposures (percutaneous or mucosal exposures) to macaques carry a real risk of exposure to B Virus since infected animals shed the virus intermittently.

This section provides a brief summary of preexposure measures and reviews the immediate clinical measures that should be taken when a person is bitten or sustains a percutaneous or mucosal exposure to a nonhuman primate. It also provides indications for prophylactic antiviral treatment.

3.1 PREVENTION (PREEXPOSURE) MEASURES

In the general population

In addition to B Virus, several other diseases can be transmitted by nonhuman primates. The most important prevention measure consists of warning the general population never to approach nonhuman primates, whether in zoos, amusement parks, or in the wild. Section 5.1 provides more in-depth information about general prevention measures.

In the workplace

Specific preventive measures related to operational practices and protective equipment are recommended by a variety of organizations that oversee the use of laboratory animals, including nonhuman primates. These measures are listed in section 5.2.

3.2 IMMEDIATE CLINICAL MEASURES

Table 3 (page 14) summarizes the measures that must be taken immediately when a person is exposed to a nonhuman primate.[2] A more detailed description of these measures is provided after the table.

[2] An significant exposure is defined as: percutaneous contact (e.g., a bite, scratch or contact with a wound) or contact between a mucous membrane and the bodily fluids of a nonhuman primate, including feces.

Table 3 Summary of immediate clinical measures

First aid (see 3.2.1) within 5 minutes of exposure
Skin exposure: wash the wound with proviodine, chlorhexidine (4%), or soap and water for ≥15 minutes
Mucosal exposure: rinse the eyes or mucosa with a sterile saline solution or water for 15 minutes
Initial assessment of exposed person (see 3.2.2)
Determine whether appropriate first aid care was provided and repeat cleansing.
Obtain a detailed history of the exposure (date, time, site, type of injury sustained, biological fluids implicated).
Evaluate the patient's general state of health (including a complete physical examination and a list of the medications the patient is currently taking).
Verify tetanus vaccine status.
Determine whether postexposure prophylaxis for rabies is required.
Determine whether antibiotic prophylaxis is required.
Determine whether B Virus prophylaxis is required.
Initial assessment of nonhuman primate (see 3.2.3)
If possible, determine the species of the implicated primate, the circumstances of the exposure, the availability of the animal and its health status.
If the animal is available, request that it be examined by a veterinarian.
Laboratory testing (see 3.2.4)
Human: in the event of an significant exposure, consider obtaining baseline serum for future analysis. This specimen should be retained and analyzed only if a second serum specimen is taken. A specimen for viral culture should not be taken immediately after exposure, but only if postexposure lesions appear.
Nonhuman primate: consider having specimens taken by a veterinarian, particularly if oral or genital lesions consistent with B Virus infection are present or if prophylactic treatment is prescribed for an exposed person.
Education (see 3.2.5)
Inform the patient about signs and symptoms to look for (particularly with respect to B Virus infection – see Appendix 6) and provide the telephone number and contact information of a care facility as a precaution.
Follow-up of exposed persons (see 3.4)
Treatment (see 3.5)
Determine the need for antibiotic prophylaxis or antibiotic treatment (see 3.2.2).
Determine the need for postexposure prophylaxis for B Virus (see 3.3).
Initiate treatment if patient presents with symptoms of B Virus infection (see 3.5).

3.2.1 First aid

As with any injury, appropriate first aid care is the first measure that should be applied. This limits contact time with the biological fluids of the nonhuman primate and minimizes the risk of transmission of infectious agents. Prompt and thorough cleansing of the wound and mucosa is the most important factor in reducing the risk of B Virus infection (Holmes et al., 1995; Cohen et al., 2002) and the risk of contracting the rabies virus.

First aid must be provided for any percutaneous significant exposure (e.g., bite, scratch, contact with broken skin) or any mucosal exposure to the bodily fluids, tissues or feces of a nonhuman primate. In the case of contact with healthy, unbroken skin, regular hand washing with soap and water is deemed sufficient.

Percutaneous exposure

Within 5 minutes of exposure and for at least 15 minutes (time with a watch):

- clean the exposed area and irrigate abundantly. Washing must be painstaking and thorough;
- use proviodine or chlorhexidine (4%); otherwise, use any soap that is immediately available. Ensure thorough contact between the disinfecting solution and the wound (Cohen et al., 2002).

Mucosal exposure (eyes, nose, mouth)

Within 5 minutes of exposure, irrigate the wound thoroughly with saline solution for 5 minutes. This should be repeated two more times, at intervals of one to two minutes between irrigations.

3.2.2 Initial assessment of exposed person

After providing appropriate first aid care, the clinical interventions described below should be carried out, depending on the assessment of the situation. It is strongly recommended that the patient present at emergency to receive this care. The physician who assesses the patient must first establish the conditions of exposure (date, time, site, type of wound or other exposure, and bodily fluids implicated) and determine whether appropriate first aid care was provided. An epidemiological investigation questionnaire like the one provided in Appendix 2 should be completed.

A physical examination, an evaluation of the exposure site and a neurological examination should be completed.

Examination of the wound

Debridement

The wound should be cleansed and any devitalized, dead or damaged tissue or foreign body removed.

Cleansing of the wound should be repeated for a period of 15 minutes if the initial cleansing was not performed in a care setting or if it is unclear whether cleansing recommendations were followed.

Wound closing

This is a highly controversial subject in the literature. Generally speaking, a primate bite wound should not be closed (no stitches or steristrips) unless the wound is located on the face (esthetic reasons), where fewer infectious complications are reported. Instead, a dry bandage should be used, without the prior application of topical ointment.

X-rays

X-rays may be indicated in order to determine the presence of gas, foreign bodies or fractures.

Elevation

Elevation of the affected limb or body part is recommended; failure to elevate constitutes the most frequent cause of treatment failure. Severe wounds to the hands require immobilization.

Specimen collection

Specimens for serological testing

Collection of early or baseline serum should be done as soon as possible, but only after the wound has been rigorously cleansed. Baseline serum is necessary for subsequent comparison with late serum (collected four to six weeks later). The results may variously indicate that treatment needs to be initiated or that ongoing treatment needs to be maintained. The procedure for laboratory tests is described below (see section 3.2.4).

Specimens for viral culture

The collection of specimens for viral culture immediately after exposure is not recommended since this can delay wound cleansing; swabbing can also cause the virus to penetrate the wound more deeply. Deep cleansing of the wound should significantly reduce the infectious load at the exposure site and therefore reduce the need to collect specimens for viral culture.

This guide does not recommend the systematic collection of human specimens for viral culture following exposure. However, if compatible lesions appear postexposure, specimens should be taken from these lesions.

Specimen collection for bacterial culture

Specimen collection is not indicated immediately after exposure, but may be needed when the patient is reexamined if signs of bacterial infection are present.

Antibiotic prophylaxis or antibiotic therapy

Antibiotic prophylaxis or antibiotic therapy is recommended for moderate to severe wounds or wounds located on the extremities (the hands in particular).

- Principle

  The antibiotic selected should cover the primate's entire oral flora.

- Antibiotic options

  The following non-exhaustive list is proposed for information purposes only, since there are many different pathogens, including those found in the oral flora of primates, which are composed of aerobic and anaerobic bacteria. The choice, duration and route of administration of an antibiotic will depend on whether the purpose is prophylaxis or treatment (adjust according to the pathogens identified in the culture).

  - Administration by mouth:
    a) First choice: Amoxicillin-clavulanate (clavulin);
    b) Alternative: Doxycycline:

       If the person is allergic to penicillin, but this antibiotic is contraindicated in young children and in pregnant or breastfeeding women;
    c) Other option: Consultation with a microbiologist/infectologist is recommended if other treatment is needed.
  - Intravenous administration:

    Parenteral administration of an antibiotic should be considered in the presence of:
    a) a clenched fist injury;
    b) osteomyelitis, tenosynovitis, septic arthritis;
    c) cellulitis that progresses despite the administration of oral antibiotics or is accompanied by systemic symptoms;
    d) an immunocompromised patient (diabetes, neoplasia, chemotherapy or radiotherapy, HIV infection, etc.).

- Duration of antibiotic prophylaxis: 5 days.
- Duration of antibiotic therapy: 10 to 14 days, except in the presence of osteomyelitis or septic arthritis (prolong accordingly).

Immunization

There are no vaccines or specific immunoglobulins to prevent human B Virus infection. Postexposure prophylaxis for tetanus and rabies is recommended, according to the guidelines in force. In certain specific circumstances, prophylaxis for hepatitis A (see section 4.5) and hepatitis B (section 4.6) may be advisable.

Antivirals

The decision to use antiviral post-exposure prophylaxis (BV-PEP) to prevent B Virus infection should be based on the actual established risk of having contracted B Virus. Section 3.3 offers recommendations concerning antiviral post-exposure prophylaxis.

3.2.3 Initial evaluation of the nonhuman primate

Algorithm 1 (page 25) is designed to facilitate evaluation of the B Virus carrier status risk of different primates.

When evaluating a given exposure, the physician should attempt to determine the species of the implicated primate, its country of origin, the circumstances of the accident, and the availability of the animal for the purposes of veterinary assessment.

In cases of exposure to a nonhuman primate in a work setting or in captivity (e.g., research laboratory or zoo), it is important to determine the animal's medical history, including its serological status with respect to B Virus and simian immunodeficiency, the presence of herpetic lesions, any recent stress or mating, the animal's general state of health, etc. If the animal is available, it should be examined by a veterinarian, taking all necessary precautions to prevent exposure. Appendix 5 provides information on the different professionals who have a role to play in evaluating the health status of implicated nonhuman primates, along with information on the collection, forwarding and retention of animal specimens.

3.2.4 Laboratory testing

Human specimens (serology, viral culture)

Indications

If PEP is recommended or anticipated following an exposure[3] (see section 3.3) taking a baseline serum specimen is also recommended. The specimen should be collected as soon as possible, but only after rigorous cleansing of the wound, if cleansing is indicated. The serum should be stored for potential future analysis.

In persons who manifest unusual signs or symptoms suggestive of B Virus infection (see Table 2), a second serum specimen should be collected as soon as possible after the symptoms manifest, for purposes of analysis and comparison with the baseline serum. If symptoms appear less than three weeks after exposure, a third serum specimen should be collected 21 days or more after exposure, since the second specimen may have been taken too early to detect the presence of specific antibodies.

If the nonhuman primate's serology or viral culture is positive, a second serum specimen should be taken from the exposed person three to six weeks after the first specimen even in the absence of symptoms. A positive result (presence of specific antibodies) on the second or third serum specimen calls for a clinical reassessment of the patient and may require the initiation of curative treatment for B Virus infection.

The collection of culture specimens after wound cleansing is a controversial subject. Some authors argue that isolation of B Virus in such specimens may indicate residual contamination and an increased probability of infection. No positive viral culture has ever been documented in such cases. Other authors are opposed to specimen collection for the purpose of viral isolation and argue that the risk of forcing viral particles (that may remain after cleansing) more deeply into the wound is too great. However, the likelihood of finding infectious viral particles on a wound that has been properly cleaned appears to be low. It has also been argued that swabs can transfer traces of detergent solution into the transport

[3] An exposure is defined as: percutaneous contact (e.g., a bite, scratch or contact with a wound) or contact between a mucous membrane and the bodily fluids of a nonhuman primate, including feces.

medium and interfere with culturing. Finally, transportation can affect the viability of viral particles.

This guide does not recommend the systematic collection of human specimens for viral culture following exposure. However, if compatible lesions appear postexposure, specimens should be taken from these lesions.

Information required when submitting specimens

If laboratory testing is indicated (e.g., positive culture in the nonhuman primate, presence of suggestive clinical signs or postexposure lesions in the patient), acute phase and convalescent phase serum specimens and specimens for viral isolation should be forwarded to a specialized laboratory, either directly by the requesting laboratory or through the Laboratoire de santé publique du Québec (LSPQ) (see Appendix 3). The specimens should be accompanied by a requisition that provides relevant clinical information, namely:

- the patient's name;
- the patient's health insurance number;
- the type of injury sustained (bite, scratch, needlestick, other);
- any symptoms present;
- the date of the injury;
- information (species, origin…) on the nonhuman primate (if available);
- the nature of the specimen(s);
- the date the specimens were collected;
- the name and contact information of the attending or consulting physician who ordered the tests.

Information on resource persons and on the collection, forwarding, transportation and retention of specimens is provided in Appendices 3 and 4.

Simian specimens (serology, viral culture)

Background

If the nonhuman primate is available, the attending physician (in cooperation with the DSP physician) may request that the animal be examined by a veterinarian. If the examination reveals the presence of oral or genital lesions consistent with B Virus infection or if prophylactic treatment against B Virus has been prescribed for the exposed person, the veterinarian should culture the lesions (if any) and perform a serology test. However, the veterinarian should be mindful of his or her own risk of exposure when performing these procedures.

Any information thus obtained will help the attending physician validate his or her decision or establish the need to intensify patient follow up after cessation of prophylaxis. However, since it usually takes two weeks to receive results from a contract laboratory, the exposed person's attending physician cannot afford to wait for the serology results of the implicated animal to determine a course of action.

When an institutional worker is exposed to a nonhuman primate

When a worker in a research laboratory or zoo is exposed to a nonhuman primate, the establishment's veterinarian should proceed with an examination of the animal and collect all necessary specimens. The veterinarian should then communicate the serological status of the implicated animal to the establishment's medical officer or to the patient's attending physician and forward to the latter copies of all virology tests (if herpetic lesions are present) and serology tests with respect to B Virus, if specimens were collected from the nonhuman primate (minimum wait-time of two weeks for initial results). The cost of these laboratory tests are to be assumed by the institution that owns the primate. The DSP physician and the MAPAQ veterinarian are to be consulted only if necessary. It is incumbent upon the attending physician to determine whether the patient should be referred to a microbiologist-infectologist.

Exposure of any other person to a nonhuman primate

The responsibility for postexposure monitoring of any other person exposed to a nonhuman primate falls to the attending physician. In cases where the nonhuman primate is available, the DSP will support the attending physician in requesting an examination of the implicated animal if postexposure prophylaxis is consideredor recommended (see section 3.3) or if the results of the examination could have an influence on the nature of the intervention.

When a person is exposed to a nonhuman primate in an institutional setting, the same guidelines that apply for workers should be implemented, in terms of having the animal examined by an authorized veterinarian (see preceding paragraph).

Blood tests on nonhuman primates are rarely recommended since a single seronegative result does not rule out potential B Virus carrier status. If confirmation of the animal's status is essential, a second specimen should be taken at least two weeks after the first. Viral cultures of implicated nonhuman primates should only be performed if the animal presents herpetic lesions.

Appendix 5 provides information on the different professionals who have a role to play in evaluating the health status of implicated nonhuman primates, along with information on the collection, forwarding and retention of simian specimens.

Link between nonhuman primate results and patient follow up

The figure below summarizes the relationship between the examination results of the implicated nonhuman primate and patient follow up.

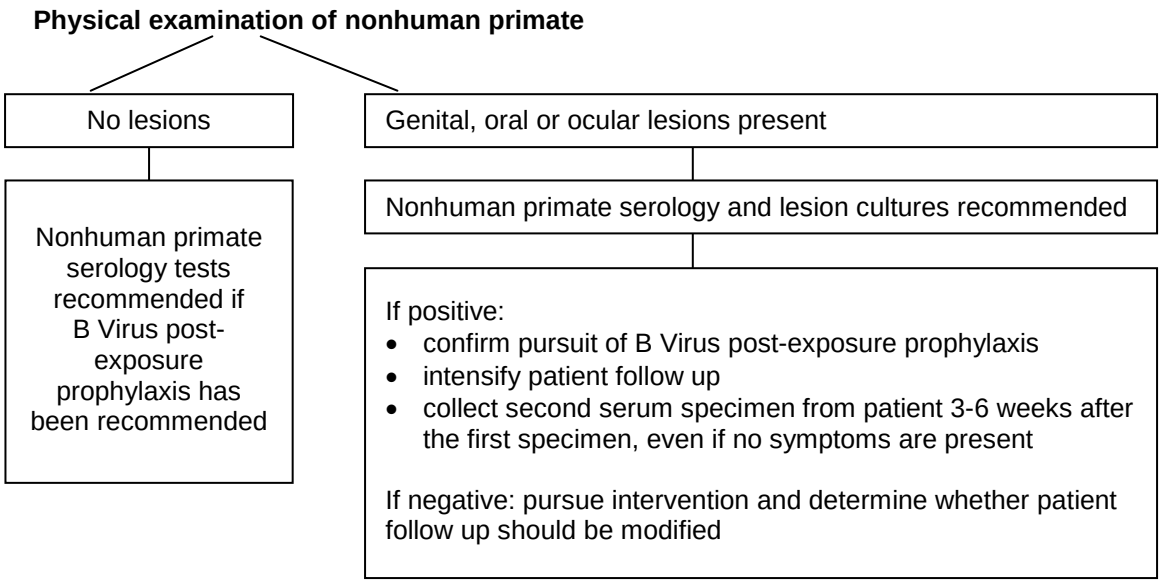


Figure 1 Physical examination of nonhuman primate

3.2.5 Education

Persons exposed to a nonhuman primate should be informed about the signs and symptoms of B Virus infection and the potential contagiosity of skin lesions (see information folder in Appendix 6). Patients should also be given a telephone number to call if they develop symptoms, as well as the contact information of a facility where they can go for prompt assessment (Appendix 7).

3.3 B VIRUS POSTEXPOSURE PROPHYLAXIS RECOMMENDATIONS

3.3.1 Decision criteria

Two algorithms have been developed to evaluate viral transmission risks and the need for prophylactic treatment.

Algorithm 1 (page 25) can be used to classify the nonhuman primate and thereby estimate the risk that the animal is a B Virus carrier.

Algorithm 2 (page 26) provides prophylaxis recommendations for different forms of exposure. Prophylaxis is not indicated if the last exposure to the nonhuman primate dates back more than six weeks (42 days), which represents twice the average incubation period of B Virus or the maximum incubation period. Algorithm 2 is based on the recommendations of a group of experts in the treatment of persons exposed to nonhuman primates (Holmes et al., 1995; Cohen et al., 2002). It outlines the situations in which postexposure prophylaxis should be considered. According to these authors, the situations in which prophylaxis is recommended are those that carry a real risk of B Virus transmission. The expert group recognizes the toxicity (however minimal) of antiviral products (see Compendium of Pharmaceuticals and Specialties of the Canadian Pharmacists Association for more details) and the drawbacks associated with their use. As a result, the group takes a nuanced approach to situations in

which the risk of transmission is minimal and merely suggests that prophylaxis be "considered" in these situations. The decision is left to the attending physician and patient. Other factors, such as the psychological and mental well-being of the exposed person, may influence the decision ultimately made (Cohen et al., 2002). Prophylaxis should always be administered to patients if it is "recommended." Indications to the effect that prophylaxis be "considered" provide more latitude to the physician, who may wish to consider the conditions of exposure, the patient's level of anxiety, etc.

The decision to prescribe prophylaxis following exposure to a nonhuman primate must be made on the basis of four important variables: **the source of the exposure, the nature of the substance to which the person was exposed, the nature of the injury, and the provision of first aid care**.

Exposure source (algorithm 1)

Only macaques are known to transmit the virus to other primates and to humans. Non-macaques are not considered to pose a risk unless they have been in contact with a macaque. Old World monkeys are at greater risk of becoming B Virus carriers than New World monkeys (see Appendix 1 and section 2.2.3). In case of exposure, the following Web site can be consulted for assistance in identifying an implicated nonhuman primate: http://www2.gsu.edu/~wwwvir/VirusInfo/macaque.html.

Nature of the substance (algorithm 2)

Exposure to fluids from an animal's oral/genital lesions, or to nerve tissue or saliva, is considered high risk. Exposure to urine, feces or blood carries a lesser risk.

Type of injury (algorithm 2)

The depth and location of the injury are important decision criteria.

Application of first aid care (algorithm 2)

Risk of infection increases if first aid care is inadequately applied since this prolongs the duration of exposure to the infectious material.

3.3.2 Algorithm-based simulations

The following simulations, which are based on algorithms 1 and 2, illustrate the decision-making process.

The simulations are presented in Appendix 9 (algorithms 2 A, 2 B and 2 C).

- A person returns from a trip to Venezuela and consults her physician as a result of having sustained a bite from a nonhuman primate that was roaming freely in the garden of her hotel. Algorithm 1 indicates that this exposure carried no risk, therefore use of algorithm 2 is not required.
- A worker injures himself (scratch with skin break) on the bars of a cage housing a seemingly-healthy macaque whose B Virus status is not known. On the basis of algorithm 2 A (Appendix 9), the application of prophylaxis should be considered.

- A veterinarian working in a laboratory housing a nonhuman primate colony sustains a stick injury from a needle previously used to draw blood from an ailing macaque. According to algorithm 2 B (Appendix 9), prophylaxis is recommended.
- A person sustains a severe bite to the hand from a macaque housed at a zoo. The animal is known to be healthy. According to algorithm 2C (Appendix 9), prophylaxis is recommended.

3.3.3 Postexposure prophylaxis

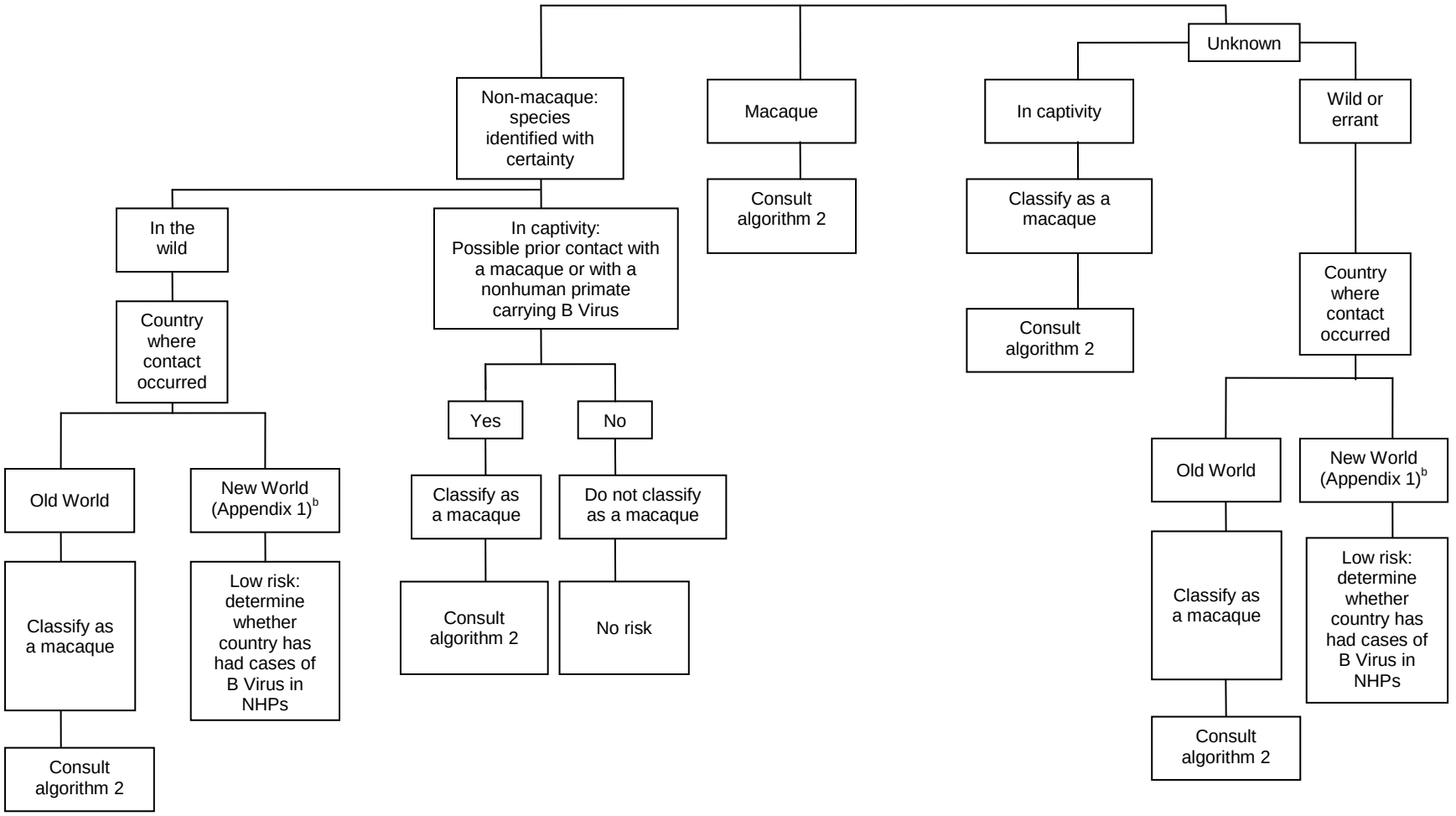
If the results of the assessment made on the basis of algorithms 1 and 2 indicate that postexposure chemoprophylaxis is required, a prescription for **valacyclovir**, 1 g, three times a day (see Table 4, p. 29) should be given to adults, with the exception of pregnant women. As a second choice, five daily doses of **acyclovir** (800 mg) can be prescribed. Acyclovir should be the first choice with pregnant women. A pregnancy test should be administered to women of child-bearing age to ensure that they are not pregnant; moreover, it is important that women not become pregnant while taking valacyclovir.

Postexposure chemoprophylaxis should be provided as soon as possible[4] after exposure, once first aid has been administered.

The recommended duration of prophylaxis is two weeks (Cohen et al., 2002). If the patient remains asymptomatic after two weeks, monitoring alone is required (see section 3.4). If the patient develops symptoms during the administration of chemoprophylaxis, intravenous treatment should be administered instead.

Table 4 (page 29) provides information on the products and dosages that should be used to treat B Virus infection or as postexposure prophylaxis (see section 3.5).

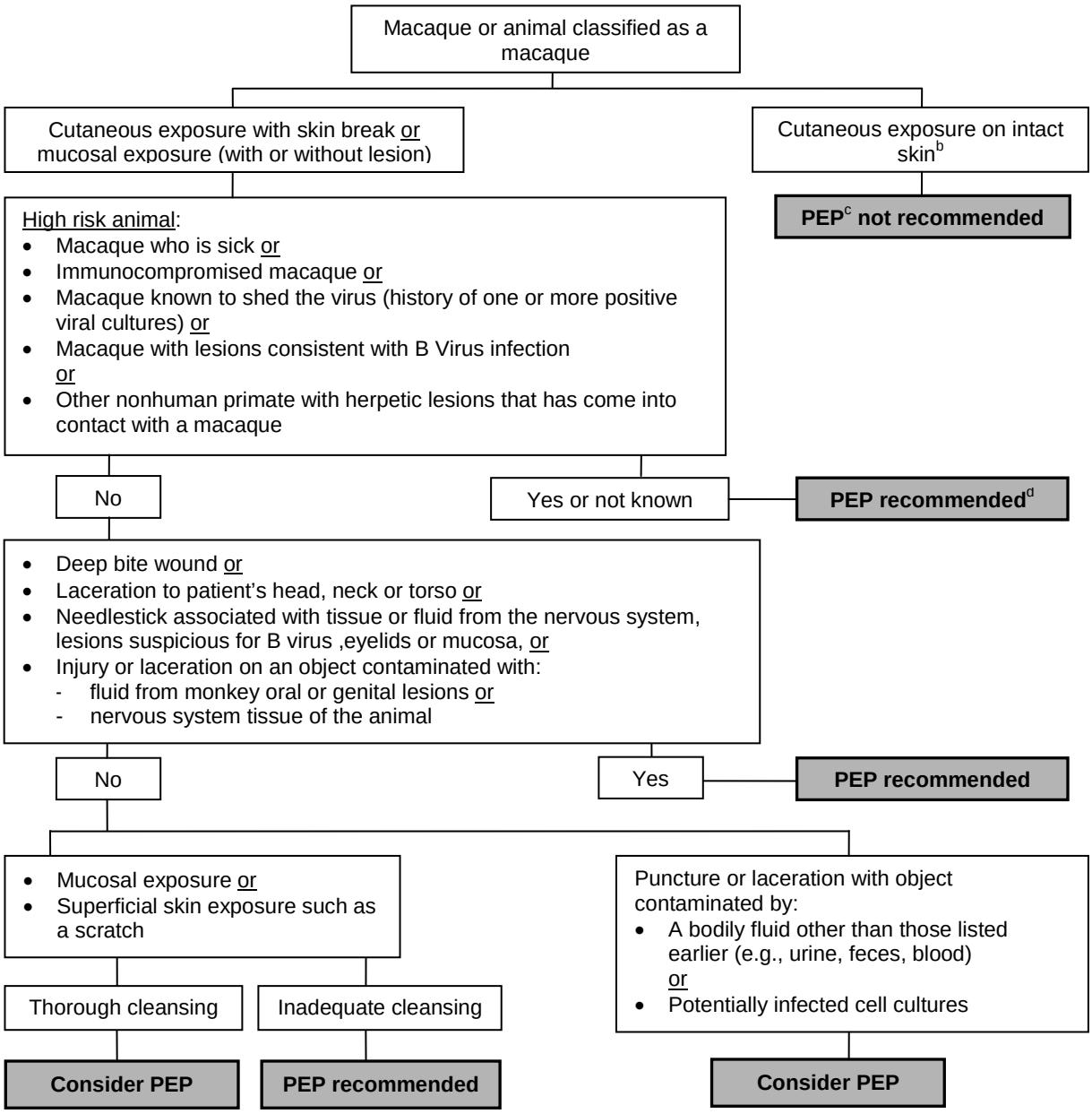
[4] Since the incubation period is six weeks, it would be unusual to initiate prophylaxis after that time.



Algorithm 1 Classification of primates in the evaluation of B Virus carrier status[a]

[a] Prophylaxis is not indicated if the last exposure to the nonhuman primate dates back more than six weeks (42 days).

[b] Nonhuman primates from Puerto Rico are considered to be B Virus carriers.



Algorithm 2 **B Virus postexposure prophylaxis recommendations**[a]

[a] B Virus prophylaxis is not indicated if last exposure with the implicated nonhuman primates dates back more than 6 weeks.

[b] If no skin lesion is evident and exposure occurred < 24 hours, wash affected area with an alcohol solution. If a burning sensation develops at the site, consider the possibility that the skin is not healthy. If exposure occurred ≥ 24 hours, evaluate the riks with the patient.

[c] PEP: postexposure prophylaxis.

[d] In the case of a macaque that is known to shed B Virus (history of one or more positive viral cultures) but is otherwise healthy and free of lesions, prophylaxis should be "considered" if a needlestick injury with blood occurs.

3.4 MONITORING OF EXPOSED PERSON

Monitoring for possible B Virus infection should include medical visits in weeks one, two and four after exposure or at any time if symptoms appear. Patients who fail to present for their appointments should be contacted by telephone. The physician following the patient should ensure that the latter is free of all symptoms of B Virus infection and is complying with prophylactic treatment if such has been prescribed.

Patients should also be given a telephone number they can call if they develop symptoms, along with the contact information of a facility where they can present for medical assessment.

It is also recommended that a nurse from the Direction de santé publique (or from a health and social services centre or family medicine group) telephone the patient for a symptom check in weeks three, five and six, or according to the arrangements made with the clinician. To that end, the physician or DSP should provide the patient with a symptom self-monitoring checklist (Appendix 7).

Depending on the nature of the wound, the physician may decide to reexamine the patient sooner and at shorter intervals (in the case of a bacterial superinfection for example).

Survival rates are higher when antiviral chemoprophylaxis is recommended and initiated promptly (Elmore and Eberle, 2008).

In the case of patients placed on antiviral chemoprophylaxis, the monitoring period should be prolonged (Cohen et al., 2002) and its duration evaluated on an individual basis by the clinician.

When a patient presents with symptoms, an investigation (including a physical examination) should be done, with particular attention given to the presence of lesions and the patient's neurological condition. The following laboratory tests should also be performed:

- cultures of all lesions (applying rigorous safety practices, since the lesions should be considered contagious), the conjunctiva and the oropharynx, to determine the presence of B Virus;
- a second serum specimen to be analyzed alongside the baseline specimen;
- all other routine specimen tests.

Neurological tests should include a lumbar puncture, a brain MRI and an electroencephalogram (EEG) (Cohen et al., 2002). A consultation with a neurologist is recommended.

If the exposed person presents with symptoms of B Virus infection (Table 2), treatment should be initiated immediately.

3.5 TREATMENT OF B VIRUS INFECTION

The presence of signs or symptoms of B Virus infection or a positive culture necessitates intravenous treatment.

The selection of an antiviral drug should be predicated on the presence or absence of symptoms indicative of central nervous system (CNS) involvement (Table 4, page 29). In the absence of CNS symptoms, acyclovir (12.5-15 mg/kg q8h) can be administered. If CNS symptoms are present, ganciclovir (5 mg/kg q12h) is recommended. Ganciclovir can also be used in patients with no CNS symptoms given the risk of rapid viral dissemination through the central nervous system (Cohen et al., 2002).

The recent use of acyclovir and ganciclovir to treat patients in the early stages of B Virus disease (including persons with early CNS involvement) has probably been responsible for the survival of these patients. However, antiviral therapy has not been particularly effective in patients with advanced encephalomyelitis (Cohen et al., 2002).

During treatment, caregivers and visitors should take additional precautions when coming into contact with the patient's blood or bodily fluids (additional contact precautions).

Duration of treatment

Treatment should be pursued until symptoms resolve and at least two series of negative cultures are obtained at 10-14 days interval. Once treatment of the infection has been discontinued, medication should be administered for an additional 6-12 months at the prophylactic dose. Prophylactic treatment can actually be maintained for several years. This approach is based on the treatment of recurrent herpes, but the treatment plan should be tailored to each situation and discussed with the patient. A consultation with a microbiologist-infectologist is recommended.

However, there are no data indicating the ideal duration of oral therapy. Treatment can be pursued for life using oral valacyclovir or acyclovir.

Table 4 Summary of medications and dosages for B Virus prophylaxis and treatment

Clinical presentation	First choice	Alternatives
Postexposure prophylaxis	Valacyclovir, 1 g PO q8h for 14 days	Acyclovir, 800 mg PO 5 times a day for 14 days
Treatment of infection • Absence of central nervous system symptoms • Presence of central nervous system symptoms	Acyclovir, 12.5-15 mg/kg IV q8h Ganciclovir, 5 mg/kg IV q12h	Ganciclovir, 5 mg/kg IV q12h

4 PREVENTION OF OTHER INFECTIOUS DISEASES TRANSMISSIBLE TO HUMANS

Other infections can also be transmitted through a significant exposure to nonhuman primates. The infections listed below are those for which exposure requires follow up and, in some cases, prophylaxis. In the case of tetanus and rabies, prophylaxis should be administered immediately.

4.1 ENTERIC DISEASES

A number of intestinal infections can be transmitted from nonhuman primates to humans and vice versa. The enteric diseases reviewed below are campylobacteriosis, salmonellosis, shigellosis, amibiasis and giardiasis.

Campylobacteriosis, salmonellosis and shigellosis

These bacterial infections manifest in captive nonhuman primates that are kept in densely populated environments. They are frequently transmitted to nonhuman primates by humans. The route of transmission is the fecal-oral route in both humans and primates. Certain nonhuman primates can be healthy carriers. Infection prevention in humans involves the application of basic sanitary practices, with a particular emphasis given to hand washing. For workers in institutional settings in which nonhuman primates are kept, the use of barriers such as gloves and personal protective clothing and equipment is recommended.

If a person presents symptoms of gastroenteritis or acute bloody diarrhea following an exposure to a nonhuman primate, a stool culture should be performed to identify potential pathogens.

Amibiasis and giardiasis

These pathogenic protozoans are endemic in nonhuman primates. Transmission to humans occurs via the fecal-oral route. The attending physician should view persistent diarrhea following contact with a nonhuman primate as potentially indicative of intestinal parasitosis. Stool examination should confirm the diagnosis. Infection can be prevented in humans by following basic sanitary practices, such as hand washing, and using personal protective equipment while working.

4.2 TUBERCULOSIS

Tuberculosis is rare in nonhuman primates living in the wild. However, primates become highly sensitive to tuberculosis and routinely acquire it in their countries of origin after coming into contact with infected humans. New World nonhuman primates are more resistant to infection that other nonhuman primates and present few symptoms when infected.

Although no cases of tuberculosis transmission from primates to humans has ever been documented, the TST- (tuberculin skin test) positive rate is 60-100 times higher among workers who handle primates than in the general population (Bennett et al., 1995).

Workers who come into contact with nonhuman primates can undergo a baseline TST, followed by another TST in 6 months and annual TSTs thereafter, depending on the level of risk posed by the colony and the nature of the contact (ILAR, 2003). When a diagnosis of tubercular disease is confirmed in a nonhuman primate, any human exposed to that primate should have a TST. If conversion occurs, the worker should be referred for medical assessment and prophylaxis should be administered if necessary.

Additional precautions (to prevent airborne transmission) should be applied by workers who handle primates during travel or during the post-import quarantine period. These precautions are in addition to the B Virus prevention recommendations that apply to personnel who work with nonhuman primates (see section 5.2).

Outside places of work, casual short-term exposure to a nonhuman primate is not considered to pose a risk of tuberculosis transmission.

4.3 TETANUS

The risk of contracting the tetanus bacterium (Clostridium tetani) from an animal bite is well known. Administration tetanus immunoglobulin and the tetanus vaccine should be evaluated according to established guidelines (see Québec Immunization Protocol, MSSS, 2004).

4.4 RABIES

Transmission of the rabies virus is a real risk, particularly with a nonhuman primate that has not been kept in captivity or for whom the period of observation (10 days) is still underway (up to six months).

Indications for prophylaxis should be evaluated on the basis of the Québec Immunization Protocol and the *Guide d'intervention provincial sur la rage humaine*. Since the period of rabies virus shedding is poorly understood in nonhuman primates, the observation period is set at six months. As a result, antirabies prophylaxis (RIG and vaccine) is commonly administered as quickly as possible after exposure.

In the case of bites and contact with saliva, appropriate first aid care (thorough, prolonged wound cleansing) is extremely important.

4.5 HEPATITIS A

Exposure to the hepatitis A virus (HAV animal variant) occurs naturally in many primate species, including chimpanzees, and owl, cynomolgus, rhesus and cercopithecus monkeys. (Bennett et al., 1995). However no cases of symptomatic human infection from these simian viruses have ever been documented (ILAR, 2003). Infections can be transmitted from human to primate in the course of capture and exportation, or through contaminated food. As a result, animals are most at risk of infection in the initial months following their arrival in the country. Only chimpanzees have ever been implicated in the retransmission of HAV human variant (ILAR, 2003). To date, over 100 cases of hepatitis A (human variant) transmission from chimpanzees to humans have been documented (Bennett et al., 1995).

Under the Québec Immunization Protocol, immunization against HAV is a preexposure indication for zoo personnel, veterinarians and researchers who work with nonhuman primates. For other persons exposed to nonhuman primates, the risk of transmission (usually through the fecal-oral route) and the need for prophylaxis should be evaluated on a case-by-case basis, with particular attention given to exposures to primates known to be sick or to have recently arrived in the country (≤ 3 months).

4.6 HEPATITIS B

Hepatitis B virus (HBV animal variant) occurs naturally in great apes such as the chimpanzee, gibbon, gorilla and, possibly, the cynomolgus monkey (*Macaca fascicularis*) (Baskin, 2002), the orangutan and the woolly monkey[5] (*Lagothrix spp*) (ILAR, 2003). The virus is fairly species-specific but is potentially transmissible to humans by these primates, even though actual transmission of the natural infection from nonhuman primates to humans has never been documented. However, hepatitis B is frequently acquired by workers who handle nonhuman primates that have been inoculated experimentally with human HBV (Bennett et al., 1995).

Workers who come into regular contact with great apes or with monkeys that have been inoculated experimentally should be vaccinated preventively against hepatitis B. In persons who have not been vaccinated, appropriate prophylaxis (specific immunoglobulin and vaccination) should be provided after any significant exposure.

Outside of institutional settings, persons significantly exposed to infectious bodily fluids of great apes or to monkeys whose species is not known but whose description is consistent with that of a large primate, should be given postexposure prophylaxis against hepatitis B on an exceptional basis.

4.7 HEPATITIS C

There is no evidence that hepatitis C virus (HCV) exists naturally in chimpanzees or other nonhuman primate species. Only chimpanzees that have been infected experimentally constitute a potential source of infection for institutional workers (Bennett et al., 1995). Other nonhuman primates have been inoculated experimentally with HCV (including cynomolgus and rhesus monkeys, African green monkeys, Japanese macaques, and baboons), but none has ever become infected or remained a carrier (Dagan et al., 1998). Certain marmoset species appear to be susceptible to HCV, but to a lesser degree than chimpanzees. However, an irregular incubation period and variable results have limited the use of this model. If an implicated animal is known to be an HCV carrier as a result of having been inoculated experimentally, the guidelines in the postexposure guide for accidental human exposure to bodily fluids (*Guide pour la prophylaxie postexposition (PPE) aux personnes exposées à des liquids biologiques dans le context du travail*, 2006) should be followed.

[5] The genus name of the woolly monkey is lagothrix.

4.8 OTHER VIRUSES

4.8.1 Herpes simplex virus

Other viruses besides B Virus are transmissible to humans. Similarly, certain viruses that are endemic in humans can cause serious infections in nonhuman primates.

Human herpes viruses 1 and 2 can be transmitted from humans to nonhuman primates (such as tamarins, marmosets and owl monkeys [Aotus] of South America). These animals are highly sensitive to human herpes viruses and infection is generally fatal for them. No transmission of herpes simplex viruses from infected primates to humans has ever been recorded in the literature. As a result of the different pathogenesis of the disease in primates, an infected animal would only be infectious for a brief period before dying.

4.8.2 Various retroviruses

It is generally acknowledged that human overpopulation has been detrimental to other animal species. As the ecological niches of many primate species become increasingly restricted or disappear entirely (in the case of species threatened with extinction), direct contact between humans and primates has increased in recent decades. Accordingly, three-quarters of all emerging diseases in recent years have been zoonoses (Wolfe, 2005).

The recent discovery that certain retroviruses can be transmitted to humans suggests that nonhuman primates carry retroviruses and possibly other viruses that are unknown to us. While we presently know very little about the pathogenesis of these infectious agents in humans, we do know that they tend to cause persistent, life-long infections.

Transmission of retroviruses following percutaneous or mucosal exposure to the bodily fluids of a nonhuman primate can be prevented by wound disinfection or mucosal irrigation similar to that recommended to prevent B Virus infection in humans.

HIV infection

We now know that HIV-1 originated with chimpanzees (Gao et al., 1999) and HIV-2 with the sooty mangabey (Cercocebus atys) (Weiss and Wrangham, 1999). Genetic sequence analysis of HIV-1 and HIV-2 (Wolfe, 2005) suggests that as many as 10 prior transmission events from primate to human occurred over the last century before HIV emerged globally.

If a person is exposed to an animal known to have been inoculated experimentally with HIV, the provincial accidental HIV exposure guide *(Guide pour la prophylaxie postexposition (PPE) aux personnes exposées à des liquides biologiques dans le contexte du travail*, 2006) should be applied. Laboratories and other settings (e.g., sanctuaries) where HIV-positive primates are known to be present should have an internal information policy and a postexposure guide that includes an agreement with a hospital prepared to deal with cases of exposure.

Simian immunodeficiency virus (SIV) infection

The epidemiology of natural SIV infection is more complex than was previously thought. A study of nine primate species indigenous to Cameroon (Aghokeng et al., 2006) found that predisposition to SIV infection varies widely from species to species.

Seroconversion has occurred in a small number of American laboratory workers who were exposed to macaques (Simian Immunodeficiency Virus-Rhesus Macaca Mulatta or SIV mac) or their bodily fluids (CDC, 1992; CDC, 1997). None of these workers developed symptoms and no sexual transmission to partners was ever documented, even in the absence of protection.

However, seroconversion is more common among people who hunt or consume the meat of nonhuman primates. A serological investigation has shown that 17% of sampled African hunters had SIV antibodies versus only 2% of city dwellers who consumed bushmeat. Although SIV has been and continues to be transmitted to humans on a regular basis, there is little or no evidence of human-to-human transmission (Wolfe, 2005).

Spumavirus (foamy virus) infection

The prevalence of foamy viruses in nonhuman primates is far greater than that of SIV. Most strains characterized to date originated in African monkeys and apes (Calattini et al., 2006). Whether acquired naturally or experimentally, the virus is non-pathogenic in nonhuman primates as a result of a very long virus-host coevolution. Natural transmission in nonhuman primates occurs primarily through bites that cause skin breaks. The presence of foamy viruses has been detected in the saliva of macaques, baboons and African green monkeys.

The first serological investigations into human foamy virus infections looked at North-American workers who handled nonhuman primates (zoo and biomedical research personnel); the prevalence rates observed ranged from 2% to 4% (Brooks et al., 2002; Sandstrom et al., 2000; Heneine et al., 1998). More recently, investigations carried out in Africans living in both forested and urban areas who had come into contact with nonhuman primates found prevalence rates of 1-2%. In hunters of monkeys and apes, however, the prevalence rate climbed to 10% (Wolfe et al., 2004; Calattini et al., 2007).

The serological and epidemiological data on transmission to humans in natural settings tend to support the hypothesis that contact between the saliva of a nonhuman primate and the blood of a human being is necessary for transmission (Calattini et al., 2007).

Clinical virological follow up of seven North American workers with foamy virus antibodies over a five-year period uncovered no infection-related pathology, nor any secondary transmission between humans, either through sexual contact or blood transfusions. (Boneva et al., 2007). Three of the seven infected workers had no recollection of percutaneous trauma caused by the implicated primate and the hypothesis of simple transmission through mucocutaneous exposure remains a possibility (Boneva et al., 2007).

The little information that is available on Africans who have seroconverted after being exposed to simian foamy viruses would suggest that infection is not associated with secondary transmission, nor with any morbidity or mortality (Wolfe et al., 2004).

Human T-lymphotropic virus (HTLV)

Two new T-lymphotropic viruses (HTLV-3 and HTLV-4) have been isolated in Africans who hunt primates or keep them as pets (Wolfe, 2005). HTLV-1 and 2 are pathogenic in humans and are related to similar viruses of simian origin.

5 GENERAL PREVENTIVE MEASURES

5.1 IN THE POPULATION

The primary recommendations that should be disseminated to the general public in order to prevent infections through contact with nonhuman primates are as follows:

- No one should ever keep a monkey as a pet (the importation of monkeys for this purpose is illegal in Canada);
- No one should ever touch or approach a monkey, be it in Québec or while travelling abroad and regardless of whether the animal is in a zoo, in the home of an acquaintance or in a public place;
- No one should ever touch with unprotected hands any object or surface (including a cage) that has come into contact with a monkey.

Additional information, including the symptoms to watch for after an exposure has taken place, can be found in the information folder presented in Appendix 6.

5.2 WORKERS

5.2.1 Responsibilities of the employer (CSST, 2003)

All employers have a responsibility to take concrete measures to prevent workplace diseases. Employers whose employees handle nonhuman primates must ensure that these employees will not become infected. In the case of nonhuman primate species of the genus macaque, the recommendations and additional protective measures set out in section 5.2.2 to prevent B Virus infection must also be applied. In addition, employers and employees must be familiar with Canadian laboratory biosafety guidelines (Health Canada, 2004). Appendix 8 provides additional information on the responsibilities and requirements that apply to employers whose employees work with nonhuman primates.

5.2.2 B Virus prevention for workers (Cohen et al., 2002; CDC, 1998)

Workers should apply the following safe work guidelines and individual protective measures:

- Macaques should only be used if the species is absolutely necessary to the work in question.
- Whenever possible the monkeys used should be free of B Virus infection and kept under appropriate conditions.
- All macaques whose serological status is unknown should be treated as if seropositive for B Virus. Handling of macaques should be as limited as possible. Capturing, restraining, immobilizing or handling a macaque that is fully awake should not be attempted; such procedures should be performed using appropriate physical and chemical restraint measures. The use of squeeze-back cages is strongly recommended. When several animals are housed together in the same cage, tunnels or chutes should be provided so that monkeys can be taken individually and restrained before handling. Positive

behavioural conditioning is helpful when removing an animal from a cage that contains several animals. Positive reinforcement consists of providing a reward (food) when the animal displays the desired behaviour.

- Handlers of particularly energetic monkeys should always wear reinforced arm-length leather gloves. They should also wear a long-sleeved protective garment to prevent scratches. Handlers who choose not to wear protective leather gloves should, at minimum, wear latex or vinyl gloves to avoid coming into contact with secretions.

- Eye and mouth protection is required during any activity that involves a risk of splashing or contact with macaque secretions or fluids (e.g., such as working in areas where macaques are kept, or capturing and transporting them in cages) (CDC, 1998). Ocular exposures in workers wearing face shields (but no protective eyewear) led authorities at the Centers for Disease Control and Prevention (CDC, 1998) to strengthen their recommendations in this regard. Earlier recommendations (CDC, 1987) dealt only with protection when removing physically active animals from cages and were therefore incomplete.
  - Type of eye and face protection:

    In their recommendations concerning basic practices and additional precautions for the prevention of virus transmission through droplets, the CDC (1998) and the MSSS (2004) recommend the use of:

    a) protective airtight goggles designed for splash protection (available with antifog lenses and lenses that preserve peripheral vision);

       combined with:

    b) a mask (surgical or procedure) that adequately protects the other mucous membranes (nose and mouth),

       or

    c) a face shield designed to (1) prevent splashes to the head from running down into the eyes and (2) adequately protect the sides and lower part of the face (to below the chin). However, this can be awkward to wear for those who work with animals, since the latter may grab or pull off the face shield.

    N.B. Corrective glasses are not considered protective equipment.
  - Situations where eye and face protection is recommended:

    In order to standardize the use of protective equipment, the Institute for Laboratory Animal Research (ILAR 2003, p. 101) specifies that eye and face protection:

    a) should be compulsory for any person working with macaques;

    b) is strongly recommended in situations that involve a risk of bodily fluid splashes from Old World monkeys and all great apes;

    c) should be evaluated for any person who works with nonhuman primates; this should involve an in-depth evaluation of workplace hazards and the determination of whether the workplace has a postexposure guide.

- Cages and other equipment that may be contaminated with B Virus must be free of sharp edges that may cause scratches or injuries to workers. Injuries sustained on cages in which virus has been shed provide a point of entry for contamination. Cages should be arranged to minimize the risk that workers will be accidentally grabbed or scratched by a

monkey. Access to the monkey housing areas should be limited at all times to workers who have received appropriate training in procedures to prevent risk of infection.

- Random selection or triaging of macaques to verify their B Virus status is not recommended. Even animals previously found to be negative may be positive at the time they inflict a scratch or bite on a worker. Moreover, such triaging may increase the risk of infection for workers. In situations where laboratory studies may cause immunosuppression in animals, the researcher may elect to determine the status of the animals to be used since virus shedding can occur under such circumstances. Macaques with oral lesions suggestive of B Virus infection should be quarantined until their lesions have healed to reduce the risk of transmission to workers or other nonhuman primates.
- Macaque handlers, including veterinarians and researchers should apply appropriate restraint measures and wear protective clothing. They should also be familiar with standard operating procedures and other prevention materials before handling monkeys. Ongoing observation should also be in place to ensure compliance with these measures. Employees should be informed of the hazards associated with scratches, bites and any other exposure to macaque secretions and the need to clean and report injuries immediately. They should also be advised that persons who are immunocompromised as a result of taking medication or having an underlying medical condition are at greater risk of contracting the virus. A pre-employment specimen should be taken from all employees hired to work with macaques and additional specimens should be taken annually for comparison in the event of an accident or suspected B Virus infection. These specimens should be stored at a temperature of -70°C.
- Workers should be told to immediately report a prolonged fever (more than 48 hours) or symptoms suggestive of influenza or B Virus infection to their supervisor and health officer, even in the absence of known exposure.
- Workers should be fully informed about the clinical signs and symptoms of B Virus infection.

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APPENDIX 1

LIST OF NEW WORLD COUNTRIES

LIST OF NEW WORLD COUNTRIES

North America

Canada
United States of America (incl. Hawaii)
Greenland
Saint-Pierre-et-Miquelon

Central America

- ***Continental Central America***

Belize
Costa Rica
El Salvador
Guatemala
Honduras
Mexico
Nicaragua
Panama

- ***Caribbean***

Anguilla
Antigua and Barbuda
Netherlands Antilles
Aruba
Bahamas
Barbados
Bermuda
Caiman Islands
Cuba
Dominica
Grenada
Guadeloupe
Haiti
American Virgin Islands
British Virgin Islands
Jamaica
Martinique
Montserrat
Puerto Rico (considered at risk for B Virus)
Dominican Republic
St. Barthelemy
St. Kitts and Nevis
St. Lucia
St. Martin
St. Vincent and the Grenadines
Trinidad and Tobago
Turks and Caicos Islands

South America

- ***Tropical South America***

Bolivia
Brazil
Colombia
Ecuador
Guyana
French Guiana
Paraguay
Peru
Suriname
Venezuela

- ***Temperate South America***

Argentina
Chile
Falkland Islands (Malvinas)
Uruguay

Sources: Wikipedia: http://fr.wikipedia.org/wiki/Am%C3%A9rique and Pan American Health Organization: http://www.paho.org/English/SHA/coredata/tabulator/newTabulator.htm.

APPENDIX 2

INVESTIGATION QUESTIONNAIRES

INVESTIGATION QUESTIONNAIRES

- Investigation questionnaire concerning a non-workplace exposure to a nonhuman primate (NHP);
- Investigation questionnaire concerning a workplace exposure to a nonhuman primate (NHP).

Agence de la santé et des services sociaux de Lanaudière
Québec

Investigation Questionnaire
Concerning a Non-Workplace Exposure to
a Nonhuman Primate (NHP)

1. Source of report

Case reported by: _____ Institution/facility: _____

Date (dd/mm/yyyy): _____ Received by: _____

2. Identification of exposed person

Name and given name: _____ Name of relative: _____

D.O.B. (dd/mm/yyyy): _____ Age: _____ Sex: ☐ M ☐ F

Address: _____

_____

Tel.: Home: ( ) ____-_____ Work: ( ) ____-_____ Cell: ( ) ___-_____

Medical history (e.g., pregnancy, kidney failure, allergies, etc.):

_____

3. Evaluation of exposure

- Date of contact (dd/mm/yyyy): _____
- City/province/country where contact occurred: _____
- Setting (work, travel, zoo, etc.): _____
- Type of NHP:
  - ☐ Macaque
  - ☐ Non-macaque (species identified with certainty):_____
  - ☐ Not known
- Type of contact
  - ☐ Bite (site) _____
  - ☐ Scratch (site): _____
  - ☐ Contact with fresh wound of patient
    - Specify type of NHP bodily fluid or substance: _____
  - ☐ Contact with mucous membrane of patient
    - Specify type of NHP bodily fluid or substance: _____
  - ☐ Needlestick injury
  - ☐ Injury involving contaminated object
  - ☐ Other type of contact (specify): _____

- Health status of NHP (if known):
  - ☐ Unwell (specify):_____
  - ☐ Immunocompromised
  - ☐ Known B Virus carrier
  - ☐ Herpetic lesions
  - ☐ Healthy
  - ☐ Other (specify): _____
- Description of event:

_____

_____

_____

_____

_____

_____

4. First aid

Was first aid provided after exposure? ☐ Yes ☐ No

If yes:

- Time between exposure and initiation of first aid care (in minutes)? _____
- First aid:
  a. For a percutaneous exposure: cleansing with soap and water (e.g., proviodine, chlorhexidine or other)?
     ☐ Yes (indicate duration): _____ ☐ No
  b. For a mucosal exposure: irrigation with saline solution?
     ☐ Yes (indicate duration): _____ ☐ No

5. Medical consultation

Was medical advice sought beforehand? ☐ Yes ☐ No

If yes, Name of physician: _____ Tel.: _____

Name of institution: _____

Date of consultation (dd/mm/yyyy):

Other consultation: _____

Treatment received: ☐ Appropriate wound cleansing (15 minutes)[6]

☐ Antibiotic therapy

☐ Antiviral (specify drug and dosage):

_____

☐ Tetanus vaccination

☐ Rabies prophylaxis

☐ Other, specify:

_____

B Virus serology performed: ☐ Yes ☐ No

6. Contact information of animal owner

- Name of animal owner or responsible organization:

  _____

- Address: _____

  _____

- Telephone: _____

7. Evaluation of animal

If animal is available

Was it evaluated by a veterinarian? ☐ Yes ☐ No

If yes:

☐ Presence of herpetic lesions noted

☐ Health status evaluated: Specify ☐ Unwell (specify) _____

☐ Immunocompromised:_____

☐ Known B Virus carrier: _____

☐ Healthy

☐ Specimen collected for serology

☐ Specimen collected for culture

☐ Results of earlier tests if known:

Serology: _____ Culture: _____

Name of veterinarian: _____ Telephone: _____

[6] See intervention guide section 3.1.

8. Surveillance of animal

If animal available for observation:

☐ CFIA (Canadian Food Inspection Agency) notified and investigation forwarded by fax on (dd/mm/yyyy) _____

☐ Observation performed by another organization (specify): _____

9. Other exposed persons

Were other persons exposed to the animal? ☐ Yes ☐ No

If yes, specify number of persons and provide their names below:

_____

10. Public health recommendations

- Medical consultation ☐ Yes ☐ No ☐ Done
- Appropriate wound cleansing ☐ Yes ☐ No
- Tetanus prophylaxis ☐ Yes ☐ TIG ☐ Vaccine
  ☐ No ☐ last dose < 5 years
  ☐ Not indicated
- Rabies prophylaxis recommended ☐ Yes (see section 11) ☐ No
- Hepatitis A prophylaxis recommended: ☐ Yes ☐ No
  If yes, specify product administered and date vaccination initiated:
  _____
- Hepatitis B prophylaxis recommended: ☐ Yes ☐ No
  If yes, specify product administered and date vaccination initiated:
  _____
- **B Virus prophylaxis:**
  ☐ Not recommended
  ☐ Should be considered
  ☐ Recommended
  - If recommended (or considered and administered):
    ☐ Baseline serum specimen of exposed human recommended and
    ☐ taken (dd/mm/yyyy): _____ or
    ☐ not taken (reason): _____
  - If considered but not administered:
    ☐ Baseline serum specimen of exposed human recommended and

☐ taken (dd/mm/yyyy): _____ or

☐ not taken (reason): _____

- Type of antiviral prescribed and dosage: (see section 11) _____

Date prophylaxis initiated (dd/mm/yyyy): _____

Date completed: _____

- **Examination of NHP recommended:** ☐ Yes ☐ No

If yes:

- Request submitted to MAPAQ on (dd/mm/yyyy): _____
- NHP examined on (dd/mm/yyyy): _____

by Dr. _____ DVM Tel.: _____

- **NHP specimens**

☐ Specimens already collected (see section 7)

☐ Specimens not collected

- Specimen collection recommended: ☐ Yes ☐ No

If yes: ☐ Collected (dd/mm/yyyy): _____

Results (date): _____

Serology: _____

Virology (if requested): _____

☐ Not collected (reason): _____

11. Postexposure prophylaxis

- **Against rabies:**

Weight: _____ Number of IU (20 IU/kg): _____

Prior rabies vaccination: ☐ Yes ☐ No

If yes, specify type of vaccine and calendar followed:

_____

Recommended calendar: ☐ RIG ☐ HDCV 5 doses ☐ HDCV 3 doses

Prophylaxis initiated (dd/mm/yyyy): _____ Location: _____

Recommended calendar - indicate projected vaccine administration dates:

Day 0 _____ day 3 _____ day 7 _____ day 14_____ day 28_____

- **Against B Virus:**

Antivirals administered: _____

Start date (dd/mm/yyyy): _____ End date: _____

12. Follow up of exposed persons

☐ Self-monitoring form provided

- Telephone follow-up:
  - ☐ Week 1: date of call: _____
    particulars:_____
  - ☐ Week 2: date of call: _____
    particulars:_____
  - ☐ Week 3: date of call: _____
    particulars:_____
  - ☐ Week 4: date of call: _____
    particulars:_____
  - ☐ Week 5: date of call: _____
    particulars:_____
  - ☐ Week 6: date of call: _____
    particulars:_____

☐ Referral for medical consultation made

Date: _____ Location: _____

13. Patient progress notes

_____

_____

_____

_____

Investigation performed by: _____ Date: _____

Agence de la santé et des services sociaux de Lanaudière
Québec

Investigation Questionnaire
Concerning a Workplace Exposure to
a Nonhuman Primate[7]

1. Source of report

Case reported by: _____ Institution/facility: _____

Date (dd/mm/yyyy): _____

Received by: _____

2. Identification of exposed person

Name and given name: _____ Name of relative: _____

D.O.B. (dd/mm/yyyy): _____ Age: _____ Sex: ☐ M ☐ F

Address: _____

_____

Tel.: Home: ( ) ____-_____ Work: ( ) ____-_____ Cell: ( ) ___-_____

Medical history (e.g., pregnancy, kidney failure, allergies, etc.):

_____

3. Identification of employer/owner of the animal:

Name of organization/employer: _____

Address of employer: _____

_____

Department in which contact with NHP occurred:

_____

Name of immediate supervisor: _____

Tel: Work: ( ) ____-_____ Cell: ( ) ____-_____ Pager: ( ) ___-_____

If applicable:

Name of institution's medical officer: _____

Address: _____

_____

Tel.: Work: ( ) ____-_____ Cell: ( ) ____-_____ Pager: ( ) ____-_____

[7] See document: *Exposure to Nonhuman Primates: Situation, Orientation and Intervention Guide*, section 3.2.4 – When an institutional worker is exposed to a nonhuman primate, page 20.

Nom of institution's veterinarian: _____

Address: _____

_____

Tel.: Work: ( ) ____-_____ Cell: ( ) ____-_____ Pager: ( ) ____-_____

4. Evaluation of exposure

- Date of contact (dd/mm/yyyy): _____
- Type of NHP: ☐ Macaque
  ☐ Non-macaque (species identified with certainty): _____
- Type of contact ☐ Bite (site): _____
  ☐ Scratch (site): _____
  ☐ Contact with fresh wound of patient
    - Specify type of NHP bodily fluid or substance: _____
  ☐ Contact with mucous membrane of patient
    - Specify type of NHP bodily fluid or substance: _____
  ☐ Needlestick injury
  ☐ Injury involving contaminated object
  ☐ Other type of contact (specify): _____
- Description of event:

_____

_____

_____

_____

_____

5. First aid

Was first aid provided after exposure? ☐ Yes ☐ No

If yes:

- Time between exposure and initiation of first aid care (in minutes)? _____
- First aid:
  a. For a percutaneous exposure: cleansing with soap and water (e.g., proviodine, chlorhexidine or other)?
     ☐ Yes (indicate duration): _____ ☐ No
  b. For a mucosal exposure: irrigation with saline solution?
     ☐ Yes (indicate duration): _____ ☐ No

6. Accident report

Completed ☐ Yes Date (dd/mm/yyyy):_____

☐ No If no, provide reason:_____

7. Medical consultation

Was medical advice sought first? ☐ Yes ☐ No

If yes, Name of physician: _____ Tel.: _____

Name of institution:_____

Date of consultation (dd/mm/yyyy): _____

Other consultation: _____

Treatment received: ☐ Appropriate wound cleansing (15 minutes)[8]

☐ Antibiotic therapy

☐ Antiviral (specify drug and dosage):

_____

☐ Tetanus vaccination

☐ Rabies prophylaxis

☐ Other (specify):_____

B Virus serology performed: ☐ Yes ☐ No

8. Evaluation of animal

- Known health status of NHP according to clinical records (information forwarded by veterinarian of institution):

  ☐ Unwell (specify): _____

  ☐ Immunocompromised

  ☐ Known B Virus carrier

  ☐ Herpetic lesions

  ☐ Healthy

  ☐ Other (specify): _____

- Was the animal evaluated by a veterinarian after exposure occurred?

  ☐ Yes ☐ No

  If yes:

  ☐ Presence of herpes lesions noted

  ☐ Specimen collected for serology

[8] See Intervention Guide section 3.1.

☐ Specimen collected for culture

Name of veterinarian (if different from institution's veterinarian):

_____ Telephone: ( ) _____-_____

9. Surveillance of animal

If animal available for observation:

☐ CFIA notified and investigation forwarded by fax on (dd/mm/yyyy) _____

Observation performed by another organization (specify):

_____

10. Other exposed persons

Were other persons exposed to the animal? ☐ Yes ☐ No

If yes specify number of persons _____ and provide their names below:

_____

11. Public health recommendations

- **Medical consultation** ☐ Yes ☐ No ☐ Done
- **Appropriate wound cleansing** ☐ Yes ☐ No
- **Tetanus prophylaxis** ☐ Yes ☐ TIG ☐ Vaccine
  ☐ No ☐ last dose < 5 years
  ☐ Not indicated
- **Rabies prophylaxis recommended** ☐ Yes (see section 12) ☐ No
- **Hepatitis A prophylaxis recommended**: ☐ Yes ☐ No

  If yes, specify product and date vaccination initiated:

  _____
- **Hepatitis B prophylaxis recommended**: ☐ Yes ☐ No

  If yes, specify product and date vaccination initiated:

  _____
- **B Virus prophylaxis:**

  ☐ Not recommended

  ☐ Considered

  ☐ Recommended

  - If recommended (or considered and administered):

    ☐ Baseline serum specimen of exposed human recommended and

    ☐ taken (dd/mm/yyyy): _____ or

    ☐ not taken (reason): _____

- If considered but not administered:
  - ☐ Baseline serum specimen of exposed human recommended and
    - ☐ taken (dd/mm/yyyy): _____ or
    - ☐ not taken (reason): _____
  - Type of antiviral prescribed and dosage: (see section 12) _____
    Date prophylaxis initiated (dd/mm/yyyy): _____
    Date completed: _____

- **Examination of NHP recommended:** ☐ Yes ☐ No

  If yes:
  - Request submitted to MAPAQ on (dd/mm/yyyy): _____
  - NHP examined on (dd/mm/yyyy): _____
    by Dr. _____ DVM Tel.: _____

- **PNH specimens**

  ☐ Specimens already collected (see section 8)

  ☐ Specimens not collected
  - Specimen collection recommended: ☐ Yes ☐ No
    If yes: ☐ Collected (dd/mm/yyyy): _____
    Results (date): _____
    Serology: _____
    Virology (if requested): _____
    ☐ Not collected (reason): _____

12. Postexposure prophylaxis

- **Against rabies**

  Weight: _____ Number of IU (20 IU/kg): _____

  Prior rabies vaccination: ☐ Yes ☐ No

  If yes, specify type of vaccine and calendar followed:

  _____

  Recommended calendar: ☐ RIG ☐ HDCV 5 doses ☐ HDCV 3 doses

  Prophylaxis initiated (dd/mm/yyyy): _____ Location: _____

  Recommended calendar, indicate projected vaccine administration dates:

  Day 0 _____ day 3 _____ day 7 _____ day 14_____ day 28_____

- **Against B Virus:**

  Antivirals administered: _____

  Start date (dd/mm/yyyy): _____ End date: _____

13. Follow up of exposed person

(by the health office of the organization/employer or the Direction de santé publique)

☐ Self-monitoring form provided

- Telephone follow-up:
  - ☐ Week 1: date of call: _____
    particulars:_____
  - ☐ Week 2: date of call: _____
    particulars:_____
  - ☐ Week 3: date of call: _____
    particulars:_____
  - ☐ Week 4: date of call: _____
    particulars:_____
  - ☐ Week 5: date of call: _____
    particulars:_____
  - ☐ Week 6: date of call: _____
    particulars:_____

☐ Referral for medical consultation made

Date: _____ Location: _____

14. Patient progress notes

_____

_____

_____

_____

Investigation performed by: _____ Date: _____

APPENDIX 3

LSPQ, MAPAQ AND NML CONTACT INFORMATION

LSPQ, MAPAQ AND NML CONTACT INFORMATION

- Laboratoire de santé publique du Québec, Institut national de santé publique du Québec:

  For all questions related to laboratory aspects of B Virus infection in humans, contact:

  Laboratoire de santé publique du Québec
  Secteur Sérodiagnostic et Virologie
  20045, chemin Sainte-Marie
  Sainte-Anne-de-Bellevue (Québec) H9X 3R5
  Tél.: 514-457-2070
  Fax: 514-457-6346

- Laboratoire de pathologie animale, MAPAQ:

  Médecin vétérinaire coordonnateur aux zoonoses
  (Dr. Chantal Vincent is the current coordinator)
  200, chemin Sainte-Foy, 11e étage
  Québec (Québec) G1R 5V7
  Tél.: 418-380-2100, ext. 3110
  Fax: 418-380-2169

- National Microbiology Laboratory:

  Public Health Agency of Canada
  1015 Arlington Street
  Winnipeg (Manitoba) R3E 3R2

APPENDIX 4

COLLECTION, FORWARDING AND RETENTION OF HUMAN SPECIMENS

COLLECTION, FORWARDING AND RETENTION OF HUMAN SPECIMENS

Specimen collection

Serum

- Collect 5-7 ml of blood in a red stopper blood collection tube with or without a serum separator.
- Allow clot to form for at least 15 minutes.
- Centrifuge specimen to separate serum from clot.
- Identify a 2-ml freezer test tube with patient's complete name and specimen collection date.
- Place 0.5 to 2 ml of serum in a leak-proof tube and ensure that cap is screwed on tightly.
- Store in serum bank at ≤ -20°C. If specimen is to be transported to an outside laboratory, transport frozen.

NOTE:	- Do not ship serum specimens in glass tubes. - Do not freeze or ship whole blood specimens. - Do not ship specimens that are improperly labelled or whose labels contain superfluous information that may cause confusion. - Do not allow serum to thaw prior to shipment.

Specimens for viral culture (if justified only)

- Identify specimen tubes with patient's complete name, the date the specimen was collected and the collection site (in English if requesting laboratory is sending specimens directly to an American reference laboratory).
- In symptomatic individuals (Table 2) collect samples from the following sites:
  - conjunctiva;
  - posterior oropharynx;
  - biopsy or swab of all papular, vesicular or ulcerative lesions consistent with B Virus infection.
- Use cotton or dacron swabs with plastic or wood shafts.
- Place each swab in a separate tube containing 1-2 ml of transport medium for viral isolation.
- Freeze each specimen at ≤ -60°C or place on dry ice until time of shipment.

NOTE:	- Do not use swabs with metal shafts. - Do not mix swab specimens. - Do not use bacteria or virus “culturettes.” - Do not use the same swab on more than one site. - Never place more than one swab in a transport medium tube. - Never use less than 1 ml or more than 3 ml of transport medium per tube for viral isolation. - Do not freeze specimens prior to shipment.

COMMENTS	- New specimens may be required if symptoms persist and viral test results are negative. - Swabs and transport medium for viral isolation can be obtained from the facility’s microbiology laboratory or from a virology laboratory that performs viral cultures.

Questions pertaining to B Virus laboratory testing should be addressed to the LSPQ, secteur Sérodiagnostic et Virologie (see Appendix 3 for contact information).

Shipment of samples

The LSPQ sends human specimens to the National Microbiology Laboratory of the Public Health Agency of Canada in Winnipeg. The latter performs the necessary serological and viral tests. Notify the LSPQ before shipping specimens.

It is important to transport diagnostic specimens in accordance with the rules in force at the LSPQ or the outside laboratory. Ship on ice or freezer packs and indicate that the specimens are for B Virus diagnosis. Specimens for viral isolation that are likely to contain B Virus must be shipped in type 1A packaging. The latter should then be placed in a tertiary styrofoam container packed with ice or freezer packs. Labelling must comply with the Transport Canada rules that apply to specimens of this kind. Labels indicating the presence of a biohazard risk and ice must be placed on the exterior container.

Retention of baseline sera

Public health setting

The specimens are collected in a health system facility. Serum specimens should be stored at ≤ -20°C for a minimum of one year after exposure. Facilities that are not physically equipped to store specimens can forward them to the Laboratoire de santé publique du Québec (LSPQ) with an LSPQ requisition. In addition to the usual information concerning the

individual, the requisition should specify the specimen collection date, the date of the exposure, and any symptoms that are present. The notation “baseline serum for future reference” should be made when testing is not immediately required. Serum specimens forwarded to the LSPQ are retained for at least two years.

Institutional or workplace setting

Any person injured by a nonhuman primate in a private sector setting (educational, pharmaceutical or other) can receive treatment within the public health system. However, when an injured worker is treated by an institutional medical officer or workplace physician, public health officials are not notified. Certain biopharmaceutical firms deal directly with the National B Virus Resource Laboratory, a U.S. laboratory that performs serology and viral isolation tests, to ensure that specimens are shipped in accordance with the rules in force in the country of destination.

Forms for the shipment of human specimens

LSPQ request form (FO-LSPQ-221)

Write “B Virus” in the section entitled “Agent étiologique présumé ou recherché” (Presumed etiologic agent) and check the appropriate option (e.g., baseline serum for future reference, antibody detection, viral culture, or nucleic acid detection) in the section “Analyse(s) demandée(e)” (Test(s) requested). In addition to the specimen collection date, indicate the conditions and date of exposure and the date symptoms first appeared.

Communication of results

Only positive results issued by the outside laboratory will be communicated by telephone to the requesting or consulting physician, upon receipt.

APPENDIX 5

ROLES OF STAKEHOLDERS IN THE HEALTH ASSESSMENT OF NONHUMAN PRIMATES AND THE COLLECTION, SHIPMENT AND RETENTION OF SIMIAN SPECIMENS

ROLES OF STAKEHOLDERS IN THE HEALTH ASSESSMENT OF NONHUMAN PRIMATES AND THE COLLECTION, SHIPMENT AND RETENTION OF SIMIAN SPECIMENS

Stakeholder roles

If specimens need to be taken from a nonhuman primate, the attending physician, with the support of the DSP as needed, will communicate with the veterinarian-coordinator of zoonoses control at MAPAQ (see Appendix 3). The coordinator of zoonoses control will then communicate with the closest veterinary clinic or hospital equipped to perform this kind of specimen collection. An up-to-date list of veterinary practitioners qualified to perform nonhuman primate investigations will be provided to the coordinator of zoonoses control by the chair of the Ordre des médecins vétérinaires du Québec.

Role of the coordinator of zoonoses control

After contacting the veterinary practitioner and explaining professional fee arrangements,[9] it is incumbent upon the coordinator of zoonoses control at MAPAQ to put the owner or guardian of the animal in touch with the veterinary practitioner so that blood specimens can be taken to determine the serological status of the animal (and its virological status if it is symptomatic) with respect to B Virus.

If viral cultures of oral, ocular and genital mucosa are required, the coordinator of zoonoses control (MAPAQ) must ensure that the veterinary practitioner is in possession of the necessary swabs and transport media.

The coordinator of zoonoses control will instruct the veterinary practitioner to immediately forward an initial blood specimen to the MAPAQ animal pathology laboratory, followed by a second specimen two weeks later. On the advice of the coordinator of zoonoses control, the laboratory will then forward the specimens to the National Microbiology Laboratory of the Public Health Agency of Canada in Winnipeg (see Appendix 3).

Role of the veterinary practitioner

In order to protect both the nonhuman primate and personnel, the animal should be tranquilized throughout the entire procedure (physical examination or specimen collection). Once it has been appropriately restrained by its owner or guardian, the animal should be given an intramuscular injection (quadriceps, biceps, supraspinatus or infraspinatus) containing 10 mg/kg of ketamine. Within 5 minutes, the animal will become immobile (its muscles will stiffen). This provides a sufficient period of sedation to perform a physical examination and collect specimens. The animal should be placed in a cage during the recovery period and can be returned to its quarters once it becomes cognitively functional (approximately 45 minutes after administration of ketamine).

[9] For exposures that occur in institutional settings (research centre, zoo) fees will be charged to the institution. However, each situation will be evaluated on an individual basis.

- Examination
  - Donning gloves and a face shield (that also protects the eyes), the practitioner evaluates the animal, the primary focus being the condition of the oral and genital mucosa.
  - The presence of vesicles and ulcers is noted and immediately reported to the veterinarian of the Réseau d'alerte et d'information zoosanitaire (vet-RAIZO), MAPAQ. The vet-RAIZO communicates in turn with the attending physician and DSP and notifies the coordinator of zoonoses control at MAPAQ, since such findings are suggestive of active B Virus infection. The lesions are swabbed for viral culture.
- Specimen collection
  - Blood specimens should be drawn from the saphenous vein or the femoral vein in the area of the femoral triangle (locate femoral artery pulse).
  - Using a Vacutainer system (21-23 gauge) draw 3-4 ml of blood into a red stopper test tube with or without serum separator.
  - After a femoral puncture, maintain local pressure for several minutes to prevent bruising.
  - Allow specimen to coagulate for at least 15 minutes. Centrifuge and separate serum from clot if possible.
  - Forward specimen at refrigeration temperature (on dry ice) to the MAPAQ animal pathology laboratory as indicated by the coordinator of zoonoses control (Appendix 3).

Role of provincial and national laboratories (MAPAQ, NML, PHAC)

Specimens are centrifuged at the MAPAQ animal pathology laboratory to obtain at least 2 ml of serum. The laboratory then ships each preserved serum specimen by air in plastic tubes that are placed in a second leak-proof container packed with absorbent material. This container is placed in a styrofoam box with enough dry ice or pre-frozen ice packs to maintain a temperature as close as possible to 0°C during shipment. This styrofoam box is in turn placed in cardboard packaging.

It is important to transport diagnostic specimens in accordance with the rules in force. The regulations respecting the transportation of hazardous goods require that type 1A containers be used to transport diagnostic specimens.

Although such an investigation is highly unlikely, specimens destined for viral isolation and suspected of containing B Virus must be placed in a primary plastic container (containing viral transport medium) with the cap screwed on tightly. This primary container must be protected by a secondary container (a cylinder with a screw cap for example) that is itself placed in a third container (styrofoam) with at least 2.5 kg of dry ice or ice packs that have been pre-frozen at -70°C. Swabs, along with an appropriate culture medium, are to be forwarded by the provincial laboratory (MAPAQ) to the veterinary practitioner responsible for collecting the specimens. The National Microbiology Laboratory (Public Health Agency of Canada) in Winnipeg must be notified in advance that simian specimens are to be shipped, so that it may proceed with the preparation of cell cultures for viral isolation.

Communication of results

The National Microbiology Laboratory in Winnipeg faxes and mails the results to the coordinator of zoonoses control at MAPAQ, who, in turn, promptly forwards them to the attending physician and the DSP. The coordinator also communicates the results to the vet-RAIZO and the veterinary practitioner, who updates the medical record of the implicated animal accordingly.

APPENDIX 6

INFORMATION FOLDER ON THE PREVENTION OF PRIMATE-TRANSMITTED DISEASES

INFORMATION FOLDER ON THE PREVENTION OF PRIMATE-TRANSMITTED DISEASES

MONKEYS SHOULD BE HANDLED WITH GREAT CARE – THEY CAN TRANSMIT SERIOUS INFECTIONS!

If you are planning a trip to a country where monkeys roam freely, it is important to know that these animals can transmit serious infections. Monkeys may resemble humans and may seem cute and cuddly, but they should never be approached, whether in zoos, parks or in the wild. Rabies (in wild monkeys) and B Virus are some of the serious infections that can be transmitted by monkeys.

B VIRUS PREVENTION

Monkey-to-human transmission of B virus infection can be fatal.

B Virus in monkeys

The virus is primarily transmitted by macaques but no monkey is safe from this infection. B Virus infection is not obvious in macaques since the latter experience no manifestations of disease. This is why the preventive measures outlined in this folder apply to all monkeys.

- ***How is B Virus transmitted to humans?***

  A person can be exposed if:
  - bitten by a monkey;
  - scratched by a monkey;
  - the bodily fluids or feces of a monkey come into contact with the person's mucosa or non-intact skin (e.g., unhealed wound, dermatitis or eczema);
  - pricked or cut by an object that has been contaminated by a monkey (cage, bedding).

- ***How can B Virus infection be prevented?***
  - No one should ever keep a monkey as a pet (the importation and sale of monkeys for this purpose is illegal in Canada).
  - No one should ever touch or approach a monkey, whether in Québec or while travelling abroad. Persons who work with nonhuman primates should apply recommended protective measures.
  - No one should ever touch with unprotected hands any object or surface (including a cage) that has come into contact with a monkey.

- ***What measures should be taken if a person is exposed or injured?***

  As with any injury, the first step is to provide appropriate first aid care.

  First aid

  If a person has been exposed to a monkey (as described above), it is important to apply the following first aid measures.

Injury or exposure involving non-intact skin:

- **Clean the wound thoroughly and rinse abundantly as soon as possible and for at least 15 minutes (time with a watch);**
- **Use any soap that is immediately available.**

Mucosal exposure (eyes, nose, mouth, lips)

- **Rinse abundantly with water for at least 15 minutes (time with a watch).**

It is important to determine the origin of the implicated monkey – was it being kept in captivity or was it living in its natural habitat? The owner should be questioned about the animal's species and region of origin.

RABIES PREVENTION

Rabies is a potentially fatal disease that is most often transmitted through a bite or lick from an infected animal that is shedding the virus in its saliva. Monkeys in the wild may carry rabies. The first aid measures indicated above apply; however, vaccines are also available and may be necessary.

TETANUS PREVENTION

Any wound or bite inflicted by a monkey can be contaminated by the bacterium that causes tetanus. It is important to ensure that tetanus immunization is up-to-date.

HUMAN B VIRUS INFECTION

IN HUMANS, B VIRUS INFECTION PRODUCES SYMPTOMS BETWEEN THE SECOND DAY AND SIXTH WEEK OF EXPOSURE. THE MANIFESTATIONS OF B VIRUS INFECTION MAY INCLUDE:

EARLY SYMPTOMS
1. Eruptions (small blisters container clear fluid) at or near the exposure site. Care should be taken: these lesions may contain B Virus 2. Intense pain or itching at the exposure site 3. Presence of painful nodes (bumps) in the neck, groin or underarm areas (nearest to the site of exposure)
DURING THE COURSE OF THE ILLNESS
1. High temperature 2. Numbness, tingling or decreased sensitivity at or near the exposure site 3. Muscular fatigue or paralysis of the exposed limb 4. Conjunctivitis (eye inflammation) 5. Persistent hiccup
LATE SYMPTOMS (IF INFECTION LEFT UNTREATED)
1. Sinusitis 2. Neck stiffness 3. Headache lasting more than 24 hours 4. Nausea and vomiting 5. Blurred vision 6. Difficulty swallowing 7. Vertigo 8. Major weakness on the side of the body opposite the exposure 9. Loss of coordination 10. Decreased sensitivity on the side of the body opposite the exposure 11. Loss of consciousness 12. Mental impairment 13. Inability to urinate 14. Respiratory difficulty 15. Seizures 16. Progression toward complete paralysis and coma 17. Death
TO AVOID RISK OF EXPOSURE TO INFECTIOUS DISEASES: **NEVER APPROACH OR TOUCH A MONKEY!** **IF YOU WORK WITH MONKEYS, TAKE THE NECESSARY PRECAUTIONS. LEARN ABOUT PRECAUTIONS BY CONSULTING YOUR EMPLOYER OR YOUR PUBLIC HEALTH BRANCH.**
IF YOU ARE EXPOSED TO A MONKEY, SEE A DOCTOR IMMEDIATELY TO AVOID GETTING SICK. THE DOCTOR WILL PRESCRIBE ANY TREATMENT YOU MAY REQUIRE. **FOR ADDITIONAL INFORMATION YOU CAN ALSO CONTACT INFO SANTÉ BY DIALING 811.**

APPENDIX 7

SELF-MONITORING FORM FOR SYMPTOMS OF B VIRUS INFECTION

WEEK 1

Self-monitoring of symptoms following a monkey bite or other exposure

NAME OF PUBLIC HEALTH NURSE: _____TEL.: _____

HOSPITAL TO BE CONTACTED IF SYMPTOMS DEVELOP**:** _____TEL.: _____

EVERY DAY: Check the boxes that best describe the symptoms you are experiencing.

Week starting (year/month/day): _____

SYMPTOMS	**DAY**						
	1	2	3	4	5	6	7
No symptoms							
• Eruptions (small blisters containing clear fluid) at or near the injury site							
• Intense pain or itching at the exposure site							
• Presence of painful nodes (bumps) in the neck, groin or underarm area							
• Fever (temperature in °C)							
• Numbness, tingling or decreased sensitivity at or near the injury site							
• Muscle fatigue or inability to move affected limb							
• Conjunctivitis (eye inflammation)							
• Persistent hiccup							
• Neck stiffness							
• Headache that lasts more than 24 hours							
• Nausea and vomiting							
• Blurred vision							
• Difficulty swallowing							
• Vertigo							
• Major weakness on the side of the body opposite the injury							
• Loss of coordination							
• Decreased sensitivity on the side of the body opposite the injury							
• Loss of consciousness							
• Inability to urinate							
• Respiratory difficulty							
Other symptoms: specify:							

WEEK 2

Self-monitoring of symptoms following a monkey bite or other exposure

NAME OF PUBLIC HEALTH NURSE: _____TEL.: _____

HOSPITAL TO BE CONTACTED IF SYMPTOMS DEVELOP**:** _____TEL.: _____

EVERY DAY: Check the boxes that best describe the symptoms you are experiencing.

Week starting (year/month/day): _____

SYMPTOMS	**DAY**						
	1	2	3	4	5	6	7
No symptoms							
• Eruptions (small blisters containing clear fluid) at or near the injury site							
• Intense pain or itching at the exposure site							
• Presence of painful nodes (bumps) in the neck, groin or underarm area							
• Fever (temperature in °C)							
• Numbness, tingling or decreased sensitivity at or near the injury site							
• Muscle fatigue or inability to move affected limb							
• Conjunctivitis (eye inflammation)							
• Persistent hiccup							
• Neck stiffness							
• Headache that lasts more than 24 hours							
• Nausea and vomiting							
• Blurred vision							
• Difficulty swallowing							
• Vertigo							
• Major weakness on the side of the body opposite the injury							
• Loss of coordination							
• Decreased sensitivity on the side of the body opposite the injury							
• Loss of consciousness							
• Inability to urinate							
• Respiratory difficulty							
Other symptoms: specify:							

WEEK 3

Self-monitoring of symptoms following a monkey bite or other exposure

NAME OF PUBLIC HEALTH NURSE: _____TEL.: _____

HOSPITAL TO BE CONTACTED IF SYMPTOMS DEVELOP**:** _____TEL.: _____

EVERY DAY: Check the boxes that best describe the symptoms you are experiencing.

Week starting (year/month/day): _____

SYMPTOMS	**DAY**						
	1	2	3	4	5	6	7
No symptoms							
• Eruptions (small blisters containing clear fluid) at or near the injury site							
• Intense pain or itching at the exposure site							
• Presence of painful nodes (bumps) in the neck, groin or underarm area							
• Fever (temperature in °C)							
• Numbness, tingling or decreased sensitivity at or near the injury site							
• Muscle fatigue or inability to move affected limb							
• Conjunctivitis (eye inflammation)							
• Persistent hiccup							
• Neck stiffness							
• Headache that lasts more than 24 hours							
• Nausea and vomiting							
• Blurred vision							
• Difficulty swallowing							
• Vertigo							
• Major weakness on the side of the body opposite the injury							
• Loss of coordination							
• Decreased sensitivity on the side of the body opposite the injury							
• Loss of consciousness							
• Inability to urinate							
• Respiratory difficulty							
Other symptoms: specify:							

WEEK 4

Self-monitoring of symptoms following a monkey bite or other exposure

NAME OF PUBLIC HEALTH NURSE: _____TEL.: _____

HOSPITAL TO BE CONTACTED IF SYMPTOMS DEVELOP**:** _____TEL.: _____

EVERY DAY: Check the boxes that best describe the symptoms you are experiencing.

Week starting (year/month/day): _____

SYMPTOMS	**DAY**						
	1	2	3	4	5	6	7
No symptoms							
• Eruptions (small blisters containing clear fluid) at or near the injury site							
• Intense pain or itching at the exposure site							
• Presence of painful nodes (bumps) in the neck, groin or underarm area							
• Fever (temperature in °C)							
• Numbness, tingling or decreased sensitivity at or near the injury site							
• Muscle fatigue or inability to move affected limb							
• Conjunctivitis (eye inflammation)							
• Persistent hiccup							
• Neck stiffness							
• Headache that lasts more than 24 hours							
• Nausea and vomiting							
• Blurred vision							
• Difficulty swallowing							
• Vertigo							
• Major weakness on the side of the body opposite the injury							
• Loss of coordination							
• Decreased sensitivity on the side of the body opposite the injury							
• Loss of consciousness							
• Inability to urinate							
• Respiratory difficulty							
Other symptoms: specify:							

WEEK 5

Self-monitoring of symptoms following a monkey bite or other exposure

NAME OF PUBLIC HEALTH NURSE: _____TEL.: _____

HOSPITAL TO BE CONTACTED IF SYMPTOMS DEVELOP**:** _____TEL.: _____

EVERY DAY: Check the boxes that best describe the symptoms you are experiencing.

Week starting (year/month/day): _____

SYMPTOMS	**DAY**						
	1	2	3	4	5	6	7
No symptoms							
• Eruptions (small blisters containing clear fluid) at or near the injury site							
• Intense pain or itching at the exposure site							
• Presence of painful nodes (bumps) in the neck, groin or underarm area							
• Fever (temperature in °C)							
• Numbness, tingling or decreased sensitivity at or near the injury site							
• Muscle fatigue or inability to move affected limb							
• Conjunctivitis (eye inflammation)							
• Persistent hiccup							
• Neck stiffness							
• Headache that lasts more than 24 hours							
• Nausea and vomiting							
• Blurred vision							
• Difficulty swallowing							
• Vertigo							
• Major weakness on the side of the body opposite the injury							
• Loss of coordination							
• Decreased sensitivity on the side of the body opposite the injury							
• Loss of consciousness							
• Inability to urinate							
• Respiratory difficulty							
Other symptoms: specify:							

WEEK 6

Self-monitoring of symptoms following a monkey bite or other exposure

NAME OF PUBLIC HEALTH NURSE: _____TEL.: _____

HOSPITAL TO BE CONTACTED IF SYMPTOMS DEVELOP**:** _____TEL.: _____

EVERY DAY: Check the boxes that best describe the symptoms you are experiencing.

Week starting (year/month/day): _____

SYMPTOMS	**DAY**						
	1	2	3	4	5	6	7
No symptoms							
• Eruptions (small blisters containing clear fluid) at or near the injury site							
• Intense pain or itching at the exposure site							
• Presence of painful nodes (bumps) in the neck, groin or underarm area							
• Fever (temperature in °C)							
• Numbness, tingling or decreased sensitivity at or near the injury site							
• Muscle fatigue or inability to move affected limb							
• Conjunctivitis (eye inflammation)							
• Persistent hiccup							
• Neck stiffness							
• Headache that lasts more than 24 hours							
• Nausea and vomiting							
• Blurred vision							
• Difficulty swallowing							
• Vertigo							
• Major weakness on the side of the body opposite the injury							
• Loss of coordination							
• Decreased sensitivity on the side of the body opposite the injury							
• Loss of consciousness							
• Inability to urinate							
• Respiratory difficulty							
Other symptoms: specify:							

APPENDIX 8

RESPONSIBILITY OF EMPLOYERS TO PROTECT WORKERS WHO HANDLE NONHUMAN PRIMATES

RESPONSIBILITY OF EMPLOYERS TO PROTECT WORKERS WHO HANDLE NONHUMAN PRIMATES

Safe work methods

Objective

- Adopt safe work methods and techniques when working with nonhuman primates.

Means

- Develop safe work methods for all work involving nonhuman primates and keep these methods up-to-date. For example:
  - effective methods for handling and restraining nonhuman primates in order to prevent bites and other injuries;
  - safe methods for handling soiled materials or objects with sharp or cutting edges;
  - hand washing technique;
  - first aid (particularly after an exposure to the bodily fluids of a nonhuman primate);
  - personal hygiene practices in the workplace.
- Observe and analyze tasks.
- Integrate safe work methods and techniques into the tasks and duties of every employee.
- Work with personnel and the health and safety committee.

Personal protective methods and equipment (PPME)

Objective

- In the presence of biological hazards that cannot be controlled by preventive immunization, provide appropriate PPME to protect workers who handle nonhuman primates.

Means

- Identify clear, detailed PPME for each task involving nonhuman primates and each work area, after performing a stringent evaluation of the biological hazards associated with the presence of nonhuman primates (potential for bites, lacerations, oral and ocular exposure).
- Select appropriate protective equipment (gloves, protective eyewear, masks or face shields).
- Oversee the acquisition and use of protective equipment. For example:
  - adopt a purchasing policy;
  - establish an audit calendar;
  - ensure rotation of equipment kept in reserve.
- Obtain and review information materials on the protective equipment.
- Work in cooperation with the health and safety committee.

Information and training

Objectives

- Inform workers who handle nonhuman primates about the biological hazards to which they are exposed, focusing on B Virus and the different modes of pathogen transmission.
- Facilitate workers' acquisition of knowledge and skills in the prevention of biological hazards and the adoption of safe attitudes and behaviours.

Means

- Designate a person to be in charge.
- Implement the means whereby workers are to be informed about biological hazards (B Virus in particular), including the modes of transmission and clinical manifestations of B Virus infection.
- Inform workers about the first aid procedures to perform in case of exposure to the bodily fluids of nonhuman primates; demonstrate or practice these measures (Cohen et al., 2002).
- Make relevant documentation on biological hazards and PPME available to personnel.
- Train personnel in the safe performance of their tasks.
- Inform personnel about the recommended PPME for every work area in which monkeys are present.
- Train personnel in the use and maintenance of PPME.
- Maintain an up-to-date register of information and training sessions on biological hazards and PPME.
- Provide reviews on an annual basis, or whenever a worker is assigned new tasks or an exposure occurs (Cohen et al., 2002).
- Create a mechanism to inform new workers about the biological hazards to which they are exposed and provide the necessary training.
- Work in cooperation with the health and safety committee.

Postexposure action plan

A postexposure action plan should achieve two objectives:

Objective 1

- Limit the consequences of exposures to potentially infectious substances (B Virus in particular).

Means

- Establish a postexposure action plan[10] that is worded as an official institutional procedure and updated on a regular basis.
- Ensure that this official procedure is posted and known to all employees.
- Name a person (or persons) responsible for the immediate management of exposed employees.
- Ensure that a responsible person is on hand at all times and is known to all employees.
- Ensure that every resource and means required to implement the action plan is in place and up-to-date.
- Ensure that a physician, clinic or hospital is notified beforehand and is able to provide appropriate supervision of exposed workers.

Objective 2

- Rectify the situation that gave rise to the exposure and take measures to prevent similar events from happening in the future.

Means

- Designate a person to monitor cases of exposure.
- Determine the types of situations that warrant such monitoring.
- Adopt a procedure for the investigation and analysis of cases of professional exposure.
- Enter into the register of first aid care all cases of exposure and incidents that may have given rise to an occupational exposure.
- Implement follow up mechanisms.
- Work in cooperation with the health and safety committee.

[10] Postexposure action plan - role of the employer:

- Ensure ready access to first aid care, including antiseptic soap and water for thorough washing of wounds and exposed mucosa.
- Ensure that a responsible person is present at all times to:
  - assist workers in the event of an exposure;
  - ensure that first aid care is properly applied and that the appropriate health care professionals are contacted;
  - refer exposed workers as quickly as possible to the identified health services;
  - provide health care providers with all necessary information concerning the implicated NHP, including its health status, history of exposure to infectious agents, and the research work in which it is being used;
  - examine the animal to determine the presence of lesions consistent with B Virus infection;
  - take measures to have the animal tested;
  - gather information on the circumstances of the exposure;
  - once an exposed worker has been seen by the appropriate health care providers, ensure that he or she is fully aware of the signs and symptoms to watch for during the six-week period following the exposure.
- Provide appropriate administrative follow-up by:
  - conducting an investigation and analysis of exposure cases to determine their probable causes and identify corrective measures;
  - helping workers to complete necessary administrative procedures (filling out forms, obtaining medical documents, etc.);
  - providing workers with any psychological support they may require subsequent to an exposure to NHP bodily fluids, through an employee assistance program or a designated professional.

Immunization and preventive screening

Objective

- Protect workers who handle nonhuman primates against the microorganisms for which effective vaccines exist and prevent tuberculosis in workers.

Medium

- Designate a person to be in charge of immunization.
- Update workers' tetanus vaccines.
- If the risks that are present warrant it, recommend preventive HBV and HAV vaccination.
- Consider implementing annual or biennial TCT screening.

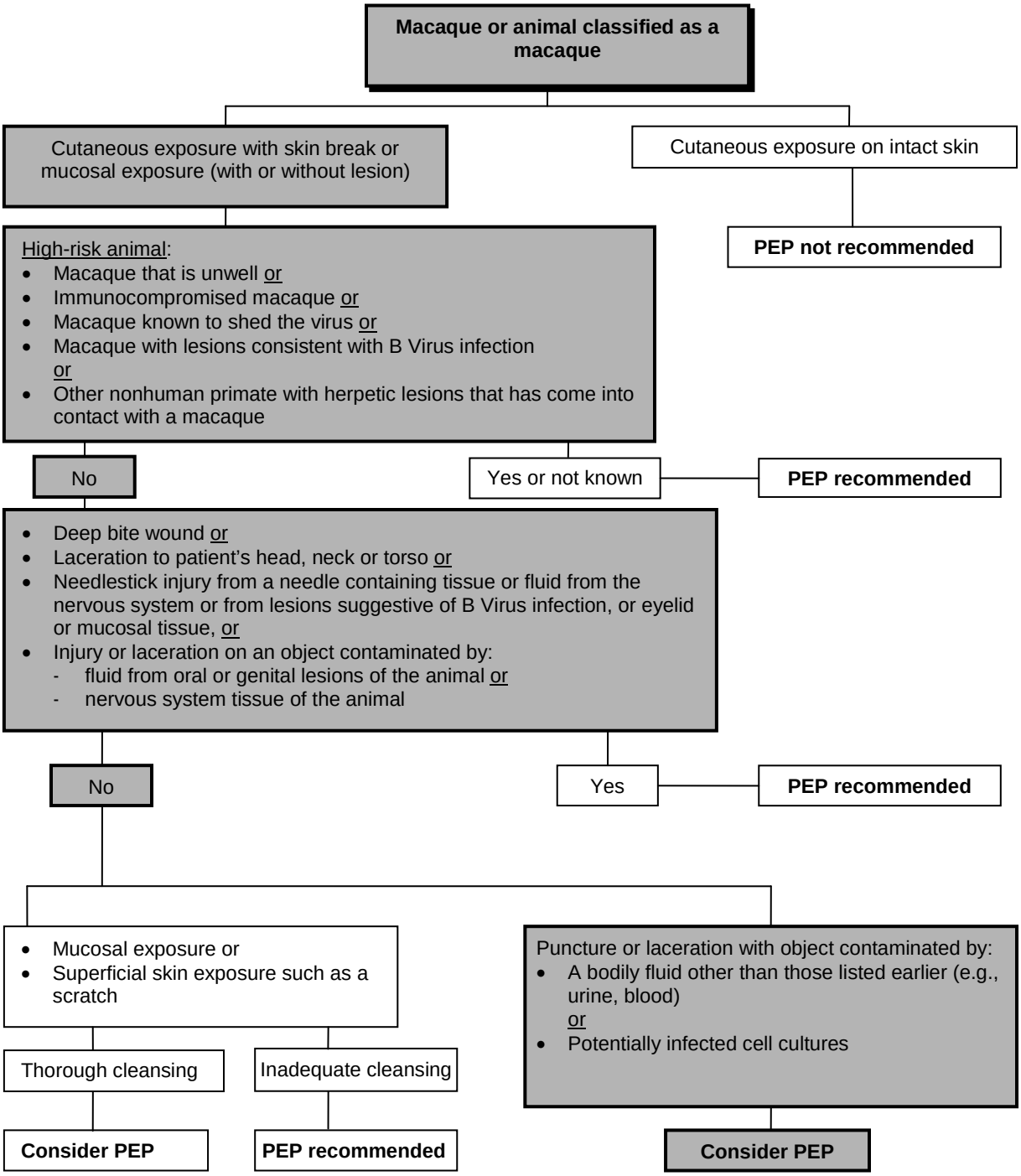
APPENDIX 9

ALGORITHM 2 INTERPRETATION SIMULATIONS

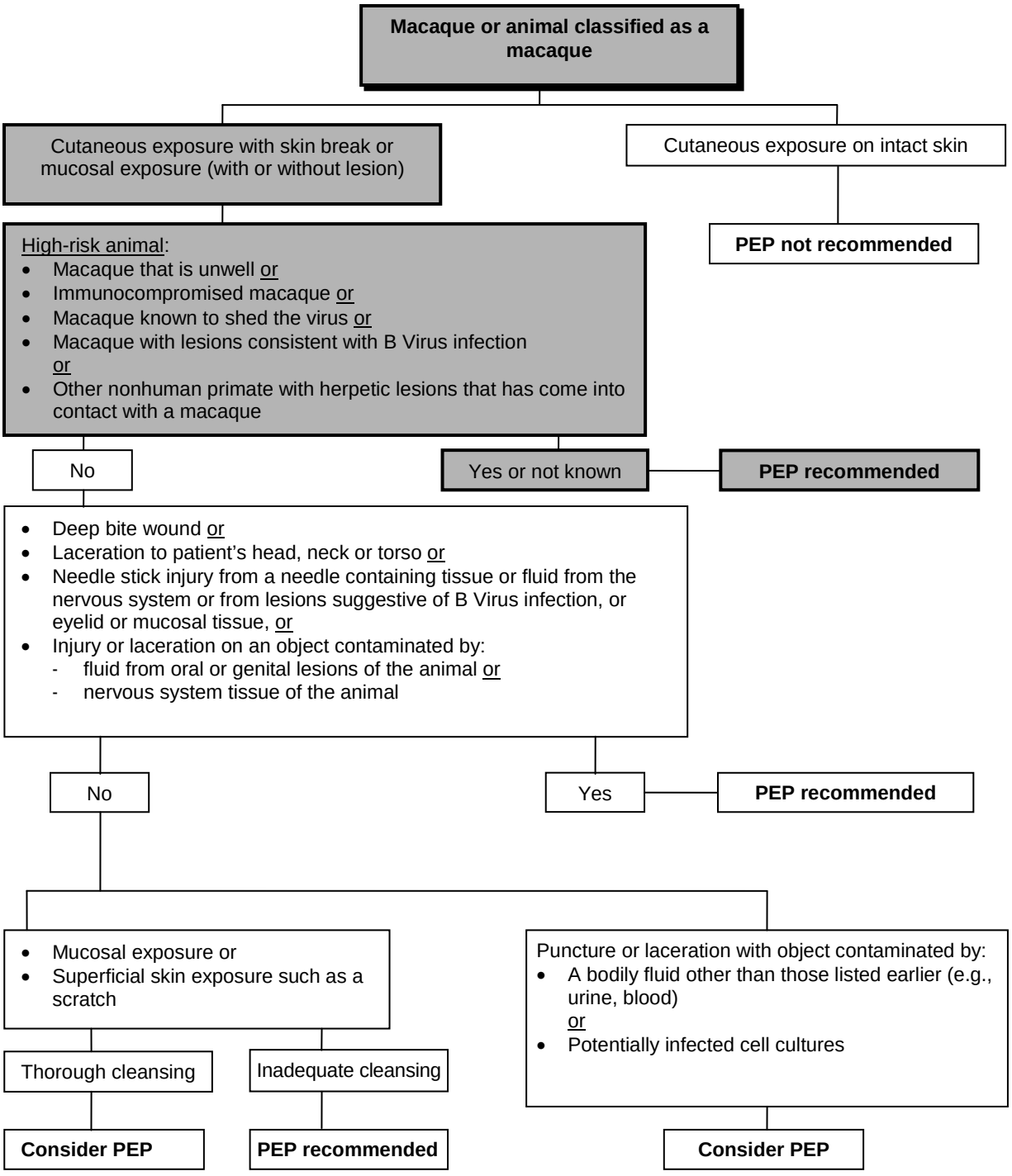
ALGORITHM 2 INTERPRETATION SIMULATIONS

Algorithm 2 reflects the decision-making sequence cited in Cohen et al. (2002). It is important to follow these steps carefully until a prophylaxis indication is reached. Algorithms 2A, B and C reproduce the case examples outlined below.

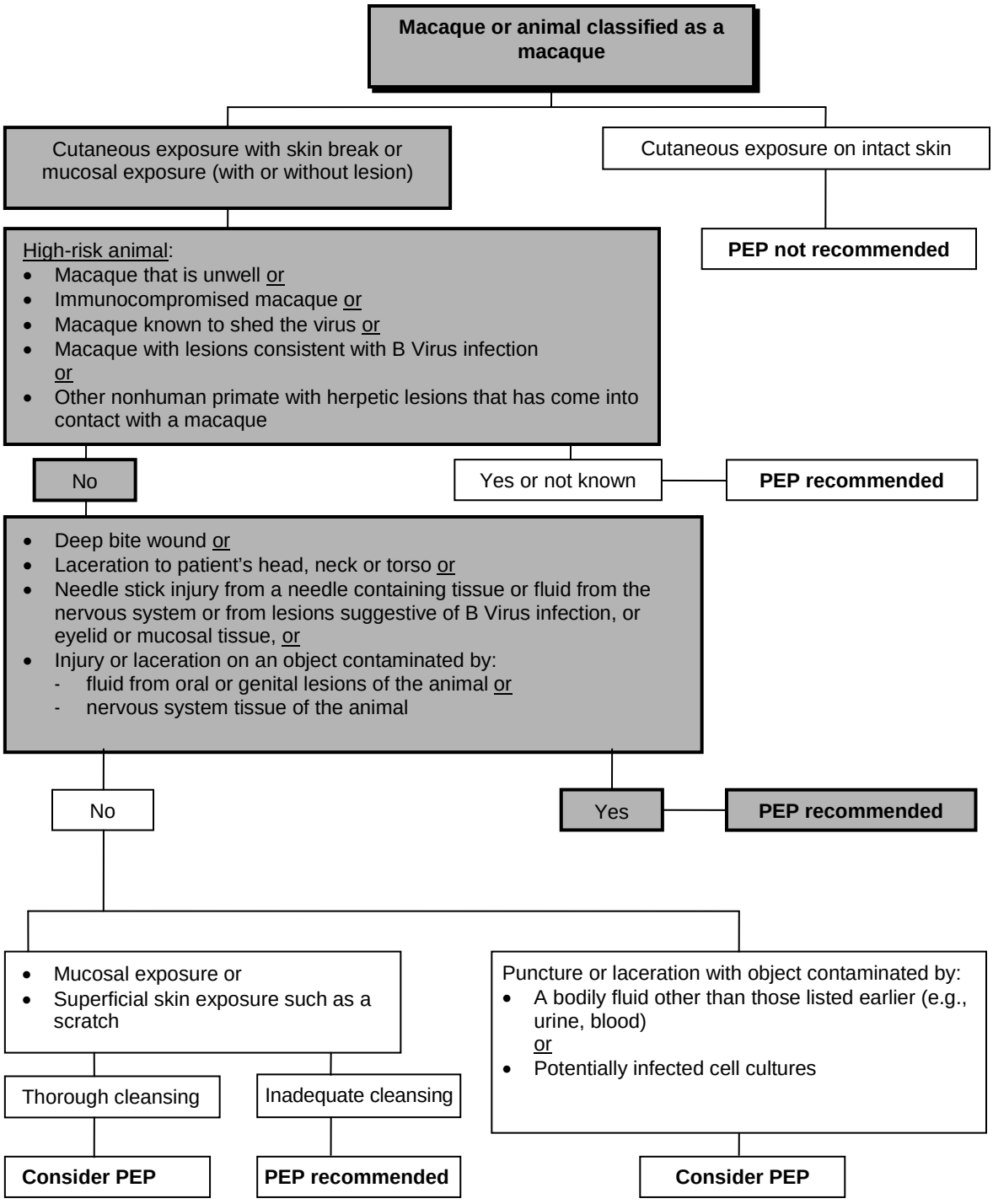
- A person returns from a trip to Venezuela and consults her physician as a result of having sustained a bite from a nonhuman primate that was roaming freely in the garden of her hotel. Algorithm 1 indicates that this exposure carried no risk, therefore use of algorithm 2 is not required.
- A worker injures himself (scratch with skin break) on the bars of a cage housing a seemingly-healthy macaque whose B Virus status is not known. On the basis of algorithm 2 A, the application of prophylaxis should be considered.
- A veterinarian working in a laboratory housing a nonhuman primate colony sustains a stick injury from a needle previously used to draw blood from an ailing macaque. According to algorithm 2 B, prophylaxis is recommended.
- A person sustains a severe bite to the hand from a macaque housed at a zoo. The animal is known to be healthy. Using algorithm 2C, it is determined that prophylaxis is recommended.



Algorithm 2 A B Virus postexposure prophylaxis recommendations



Algorithm 2 B B Virus postexposure prophylaxis recommendations



Algorithm 2 C B Virus postexposure prophylaxis recommendations

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